

POLAROGRAPHY OF SOME COORDINATION COMPOUNDS OF PLATINUM

IV. COMPOUNDS OF PLATINUM(II) CONTAINING 1,10-PHENANTHROLINE

By J. R. HALL* and R. A. PLOWMAN*

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Summary

Four ions were studied at the dropping mercury electrode. They were $[\text{Pt}(\text{ophen})_2]^{2+}$, $[\text{Pt}(\text{ophen})(\text{en})]^{3+}$, $[\text{Pt}(\text{ophen})(\text{py})_2]^{2+}$, and $[\text{Pt}(\text{ophen})(\text{py})\text{Cl}]^+$, where ophen=1,10-phenanthroline, en=ethylenediamine, and py=pyridine. The shapes of the c-v curves of the ions in supporting electrolyte 0.1M KCl, were dependent on complex ion concentration. Adsorption phenomena occurred with some ions but the effects decreased as the complex ion concentration decreased. The reduction of $[\text{Pt}(\text{ophen})_2]^{2+}$ produced evidence for compounds of platinum with valency less than two. Reduction of the other ions appeared to proceed directly to metallic platinum.

I. INTRODUCTION

This series of new compounds has been investigated in a further attempt to gain evidence for compounds of platinum(I). All the compounds contained the ligand 1,10-phenanthroline, for it was thought that this ligand might have a special influence on the stability of oxidation states of platinum less than two.

II. EXPERIMENTAL

(a) *Apparatus*.—The set-up previously described (Hall and Plowman 1955) was used. The capillary had a drop time equal to 4.8 sec and an m value of 1.50 mg sec^{-1} .

(b) *Materials*.—A.R. grade KCl was used.

(c) *Preparation of Compounds*.—(i) *Dichloro-(1,10-phenanthroline)platinum(II)*. This compound was prepared by Parsons (1954) and was used as the starting material for the preparation of the four compounds studied polarographically.

A slightly acid soln. of potassium tetrachloroplatinate(II) was brought to the boiling point and a hot aqueous soln. of 1,10-phenanthroline (ophen) slowly added. A yellow precipitate gradually deposited. The soln. was filtered hot and the precipitate washed with cold water. The compound consisted of fine needles insoluble in hot water (Found: Pt, 43.3; Cl, 15.9%. Calc. for $[\text{Pt}(\text{C}_{12}\text{H}_8\text{N}_2)_2\text{Cl}_2]$: Pt, 43.7; Cl, 15.9%).

(ii) *Bis(1,10-phenanthroline)platinum(II) Chloride 3.5-Hydrate*. This compound was first prepared by Parsons (loc. cit.). $[\text{Pt}(\text{ophen})\text{Cl}_2]$ was heated with excess ophen in aqueous soln. for 2-3 weeks. A yellow-brown soln. was obtained which yielded yellow prismatic crystals, when cooled and acidified with HCl. The product was very soluble in water but sparingly soluble in dil. HCl from which it was recrystallized. The compound was recrystallized twice more—first from dil. HCl and finally from water. The compound was insoluble in acetone which was used to wash the crystals. Decomposition commenced on heating at 100°C (Found: Pt, 28.3; Cl, 10.3%. Calc. for $[\text{Pt}(\text{C}_{12}\text{H}_8\text{N}_2)_2]\text{Cl}_2 \cdot 3.5 \text{H}_2\text{O}$: Pt, 28.3; Cl, 10.3%).

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When a slightly acid soln. of $[\text{Pt}(\text{ophen})_2]\text{Cl}_2$ reacted with a piece of magnesium or iron, considerable attenuated filamentous growth appeared on the metal. A thin iron wire took on the appearance of a hairy caterpillar. The material was very sensitive to atmospheric oxidation and appeared to regenerate the starting material in contact with the mother liquor. Attempts to isolate this compound in quantity and in a pure state have so far been unsuccessful.

(iii) *Ethylenediamine(1,10-phenanthroline)platinum(II) Chloride 2-Hydrate*. This compound was prepared by Parsons (loc. cit.). A dil. aqueous soln. of ethylenediamine (en) was warmed with $[\text{Pt}(\text{ophen})\text{Cl}_2]$ to produce a clear soln. Pale yellow crystals were deposited on adding HCl to the cooled soln. The product was recrystallized from water (Found: Pt, 36.0; Cl, 13.0%. Calc. for $[\text{Pt}(\text{C}_{12}\text{H}_8\text{N}_2)_2\text{C}_2\text{H}_4(\text{NH}_2)_2]\text{Cl}_2 \cdot 2\text{H}_2\text{O}$: Pt, 36.0; Cl, 13.1%).

(iv) *Dipyridine(1,10-phenanthroline)platinum(II) Perchlorate*. To a hot aqueous suspension of $[\text{Pt}(\text{ophen})\text{Cl}_2]$, pyridine (py) was added until the soln. cleared. On cooling and addition of sodium perchlorate soln., a pale cream precipitate was obtained. The product crystallized in the form of needles from hot water (Found: Pt, 26.6%. Calc. for $[\text{Pt}(\text{C}_{12}\text{H}_8\text{N}_2)(\text{C}_5\text{H}_5\text{N})_2](\text{ClO}_4)_2$: Pt, 26.7%).

(v) *Chloropyridine(1,10-phenanthroline)platinum(II) Perchlorate*. Pyridine was added to a hot aqueous suspension of $[\text{Pt}(\text{ophen})\text{Cl}_2]$ until the soln. cleared. The soln. was then heated on a steam-bath until the odour of pyridine was weak and crystallization commenced. The soln. on cooling, deposited a yellow crystalline precipitate. The product was recrystallized from water (Found: Pt, 33.5%. Calc. for $[\text{Pt}(\text{C}_{12}\text{H}_8\text{N}_2)(\text{C}_5\text{H}_5\text{N})\text{Cl}]\text{Cl}_3\text{H}_2\text{O}$: Pt, 33.7%). The compound decomposed at 100°C. A sample heated at 100°C rapidly lost pyridine to yield $[\text{Pt}(\text{ophen})\text{Cl}_2]$ (Found: Pt, 43.3%. Calc. for $[\text{Pt}(\text{C}_{12}\text{H}_8\text{N}_2)\text{Cl}_2]$: Pt, 43.7%). Loss of pyridine was detected from $[\text{Pt}(\text{ophen})(\text{py})\text{Cl}]\text{Cl}$ when kept in a desiccator. The chloride was dissolved in water and the soln. filtered to remove a small quantity of insoluble $[\text{Pt}(\text{ophen})\text{Cl}_2]$. The perchlorate was precipitated with sodium perchlorate and recrystallized from hot water (Found: Pt, 32.9%. Calc. for $[\text{Pt}(\text{C}_{12}\text{H}_8\text{N}_2)(\text{C}_5\text{H}_5\text{N})\text{Cl}]\text{ClO}_4$: Pt, 33.1%).

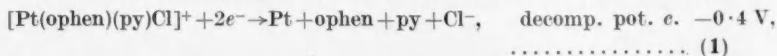
III. RESULTS AND DISCUSSION

(a) *The Reduction of $[\text{Pt}(\text{ophen})(\text{py})\text{Cl}]^+$*

Figure 1 shows the reduction of the ion at several concentrations in the supporting electrolyte, 0.1M KCl. Curves (a) and (b), representing the concentrations 0.25mM and 0.50 mM, were obtained from solutions of the perchlorate of the above cation. The solubility of the perchlorate did not allow of a 1 mM solution, so that curve (c) was obtained from a solution of the chloride of the cation. This soln. contained a small quantity of insoluble $[\text{Pt}(\text{ophen})\text{Cl}_2]$.

The curves illustrate the effect of concentration of the complex ion on reduction behaviour. Generally, reduction begins at about -0.4 V and a maximum occurs, the height changing rapidly with concentration until at 0.25 mM no maximum occurs at all. In this case, the maximum is replaced by a sharp corner in the c-v curve. After the maximum has passed, the current remains constant until -1.0 V. The current in this region seems to be diffusion controlled and is proportional to concentration of the complex ion as shown in Table 1.

When the wave height (2.6 μA) at -0.8 V for the reduction of 0.5 mM $[\text{Pt}(\text{ophen})(\text{py})\text{Cl}]^+$ is compared with the wave height (2.7 μA) for the reduction of 0.5 mM $[\text{Pt}(\text{NH}_3)_2(\text{C}_6\text{H}_5\text{NH}_2)_2]^{2+}$ (Hall and Plowman 1956), it is concluded that the limiting current region at -0.8 V results from the electrode reaction



since the same capillary was used for both reductions.

Curve (a) shows the complete reduction behaviour of the ion at a concentration equal to 0.25 mM up to the discharge of potassium ions at -2.0 V. From -1.0 V to more negative voltages, the curves for the higher concentrations

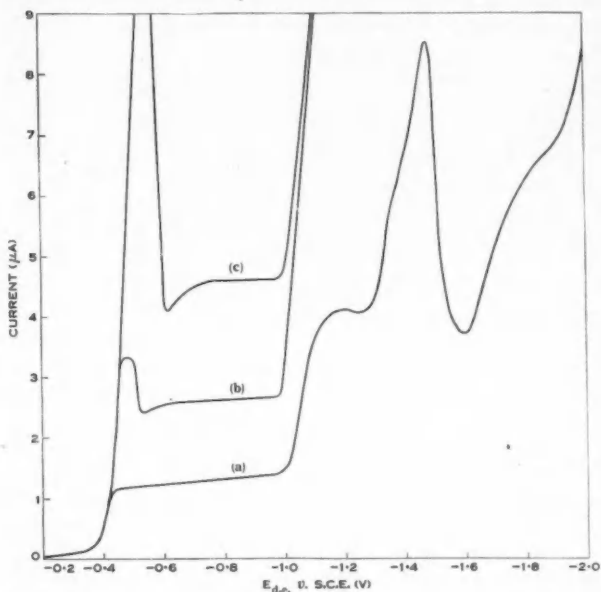


Fig. 1.—c-v curves of $[\text{Pt}(\text{ophen})(\text{py})\text{Cl}]^+$ at the concentrations: (a) 0.25mM in 0.1M KCl; (b) 0.50mM; (c) 1.0mM.

have shapes which are parallel to curve (a). That is, the curves are characterized by a small hump at -1.2 V, then a maximum, followed by a current minimum at -1.6 V. At still more negative voltages the wave due to hydrogen formation

TABLE I
POLAROGRAPHIC REDUCTION OF COMPLEX IONS

Concn. (mM)	$[\text{Pt}(\text{ophen})(\text{py})\text{Cl}]^+$	$[\text{Pt}(\text{ophen})_2]^{2+}$
	i at -0.8 V corrected for i_r (μA)	i at -0.6 V corrected for i_r (μA)
0.25	1.14	0.41
0.50	2.44	0.84
1.00	4.43	1.72

is evident, and the height of this wave depends on the concentration of the complex ion.

From -1.0 V, then, the nature of the process occurring at the D.M.E. seems to be independent of the concentration of complex ion. In the limiting

current region prior to -1.0 V, there is being liberated at the mercury drop surface, free ophen and pyridine. Unpublished work by Breyer *et al.* reported by Dwyer and Wooldridge (1949) indicates that ophen reduces in two stages, at first one electron then three adding on. The present authors have studied the reduction of ophen in unbuffered solution containing KCl and also in KCl and gelatin. The curve is difficult to interpret in the former case, but in the presence of gelatin corresponds to two successive two-electron reductions. Discharge commences at -1.1 V *v.* S.C.E.

In the reduction of the complex ion it is possible that the discharge occurring at -1.0 V is due to the reduction of liberated ophen. Because the availability of ophen at the D.M.E. is governed by the diffusion of the complex ion, it is reasonable to expect that the current due to the reduction of ophen will attain a limiting value. The hump at -1.2 V may well represent this limiting current. However, if this wave represents the reduction of ophen, governed by diffusion of the complex ion, it would be expected that the wave height would be proportional to concentration. This is not the case. The height of the wave at -1.2 V is twice the height of the wave at -0.8 V for curve (a), but for 0.5 mM, the height of the second wave is three times the height of the preceding wave. From curve (a) it is seen that a maximum occurs after the hump at -1.2 V and that after the maximum has been passed the current falls below its value at -1.2 V. As the concentration of complex ion increases the current minimum at -1.6 V falls further below the current value at -1.2 V.

It is questionable whether the wave attributed to reduction of ophen can be compared with its reduction wave in media containing no other reducible substances. The deposition of platinum on the mercury surface could substantially affect the reduction behaviour of the liberated ophen. The interpretation of the curve from -1.0 V to more negative voltages may be further complicated by the possible reduction of pyridine. Pyridine has been examined polarographically in an unbuffered acid supporting electrolyte by Kaye and Stonehill (1952). The reduction wave commences at -1.4 V *v.* S.C.E. The present authors found that pyridine has no influence on the *c-v* curve of ophen in 0.1 M KCl and 0.01 per cent. gelatin. However, the reduction of pyridine may also be affected by the presence of liberated platinum.

(b) Reduction of $[Pt(ophen)_2]^{2+}$

Figure 2 illustrates the behaviour of this ion at the concentrations 0.25 , 0.50 , 1.0 mM, in the supporting electrolyte 0.1 M KCl. In the case of curve (c), the polarogram is characterized by an extremely rapid current increase in the region of -0.41 V *v.* S.C.E. The curve then rounds off and the current approaches a constant value over 0.1 V. At -0.7 V the current increases again and while there is a slight tendency for the *c-v* curve to form another step, dropping becomes irregular and the current increases rapidly. In this region an olive-green filamentous material accumulates about the mercury drops. From the voltage when the insoluble material is first observed until the discharge of potassium ions, consistent current values for a fixed voltage setting are not registered by the galvanometer. The high current values and their irregularity are attributed to mechanical disturbance about the growing drops as the insoluble material is produced.

The height of curve (c) at -0.6 V is proportional to the height of the mercury column. This result indicates that the current is primarily due to reduction of the adsorbed complex ion. That the material is strongly adsorbed is supported by the fact that neither gelatin nor camphor had any effect on the shape of the wave.

The effect of reducing the concentration of the complex ion on the shape of the polarogram is illustrated by curves (a) and (b). As the concentration of the complex ion decreases, the voltage at which the insoluble material appears becomes more negative. The result is that a possible second wave is exposed though itself somewhat irregular in form. From -0.7 V the c-v curves are not reproducible and once the formation of insoluble material is observed there is no possibility of any interpretation of the reduction processes. Only the final surge of current due to reduction of potassium ions is distinguishable.

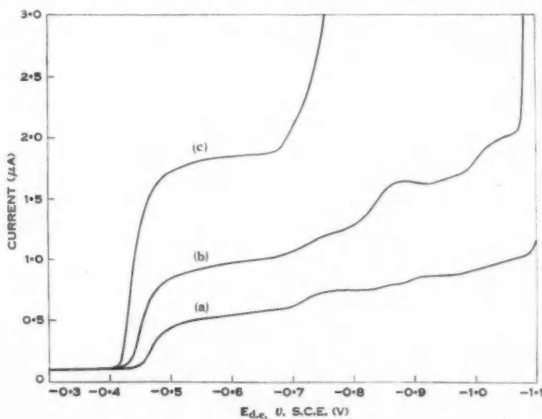


Fig. 2.—c-v curves of $[\text{Pt}(\text{ophen})_2]^{3+}$ at the concentrations: (a) 0.25 mM in 0.1M KCl; (b) 0.50 mM; (c) 1.00 mM.

It is evident from the c-v curves that proportionality exists between concentration of complex ion and current for the first step. Values of the current at -0.6 V v. S.C.E., corrected for residual current, are listed in Table 1. Also, as concentration of complex ion decreases the shape of the c-v curve approaches a more normal form. It is observed that the reduction potential becomes more negative as concentration decreases.

If it is assumed that adsorption effects are small at low concentrations, the electrode reaction will tend to be diffusion controlled at small concentrations. Because of the linear relationship between the limiting current and concentration at small concentrations of the reducible ion, the Ilkovic equation was used to calculate the number of electrons involved. From conductivity measurements made on the ion and calculation of the diffusion coefficient, a value of 0.7 for n was obtained for the reduction process at -0.6 V. Since the first step is

followed by the start of a second wave (discharge beginning at -0.7 V), it is postulated that the reduction of $[\text{Pt}(\text{o phen})_2]^{2+}$ occurs in two stages.

The second reduction stage is accompanied by the production of a fine needle-like insoluble material which is comparable to that found by reduction of the compound by magnesium or iron as described in Section II (ii). Since the first reduction wave seems to be a one-electron process and further reduction produces an insoluble compound which appears capable of being oxidized to the original ion (see Section II), it is possible that the second reduction produces a zerovalent platinum compound. The existence of a compound of platinum(0) has been postulated by Watt, Walling, and Mayfield (1953). The compound is formed by the reduction of tetrammineplatinum(II) ion by sodium in liquid ammonia.

When ophen alone is reduced at the D.M.E., and during the reduction of other platinum complexes containing ophen, no insoluble material accumulates at any time.

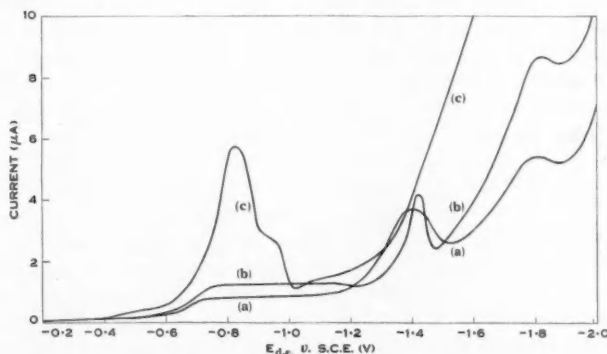
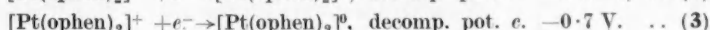


Fig. 3.—c-v curves of $[\text{Pt}(\text{o phen})(\text{py})_2]^{2+}$ at the concentrations: (a) 0.13 mM in 0.1M KCl; (b) 0.25 mM; (c) 1.00 mM.

If in the present work a zerovalent platinum compound is formed, the formula $[\text{Pt}(\text{o phen})_2]^0$ would account for the regeneration of the original compound by oxidation. Therefore it appears likely that the initial one-electron reduction produces $[\text{Pt}(\text{o phen})_2]^+$.

Further attempts are being made to substantiate these claims by isolation of definite compounds. The following tentative electrode reactions are postulated:



(c) *Reduction of $[\text{Pt}(\text{o phen})(\text{py})_2]^{2+}$*

Figure 3 shows the behaviour of this ion at various concentrations. Curve (c) for 1 mM complex ion exhibits a hump with a maximum at -0.8 V and a decrease in current at -1.0 V. The current then gradually increases until discharge at -1.3 V. At a concentration equal to 0.5 mM, the c-v curve is

similar to curve (c), except that the maximum at -0.8 V is not so high and is removed by gelatin. Hence, changing the concentration has little effect on the quantity of platinum complex reduced. A similar hump (without the maximum) is shown to occur in the reduction of $[\text{PtCl}_4]^-$ by Laitinen and Onstott (1950) and is attributed by them to adsorption and desorption of the ion.

Curves (a) and (b) show a more normal shape with dependence of current on concentration. Also, it appears that the reduction voltage is slightly greater than -0.6 V. Both curves contain a maximum at -1.4 V prior to the evolution

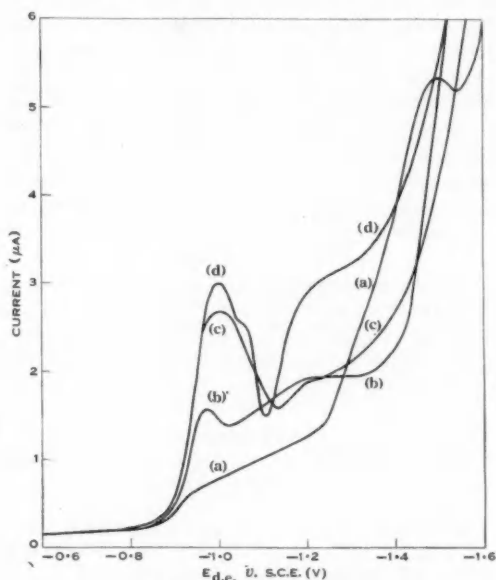
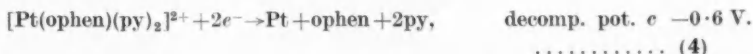


Fig. 4.—c-v curves of $[\text{Pt}(\text{ophen})(\text{en})]^{2+}$ at the concentrations: (a) 0.13 mM in 0.1M KCl; (b) 0.25 mM; (c) 0.50 mM; (d) 1.00 mM.

of hydrogen and discharge of potassium ions. In the range where current depends on concentration, comparison with the currents for reduction of $[\text{Pt}(\text{ophen})(\text{py})\text{Cl}]^+$ indicates the two-electron process



The above reduction gives rise to free ophen so that a discharge at -1.0 V would be expected as in Figure 1. Discharge does not commence until -1.2 V in Figure 3. Comparing the region from -1.0 to -1.6 V with the same region in Figure 1, no similarities are observed apart from maximum phenomena at -1.4 V. Thus there appears to be little correlation if processes occurring in the above region are to be attributed to the free ligands.

(d) Reduction of $[Pt(o\text{phen})(en)]^{2+}$

Figure 4 shows the behaviour of the ion at several concentrations. The *c-v* curve (d) for 1 mM complex ion has characteristic shape and is completely reproducible. At 0.5 mM, curve (c), the shape is different and the magnitude of the current in the region of -1.3 V is very sensitive to slight deviations in concentration from 0.5 mM. At 0.25 mM, curve (b), the maximum is very small but the current at -1.3 V is not significantly different from the current for double the complex ion concentration. Curve (a) approaches a normal polarographic shape.

When a 1 mM solution of the complex ion is reduced in the presence of free *o*phen, the maximum is almost suppressed and the initial discharge shifts to about -1.0 V. At the same time, the current recorded at -1.3 V is not enhanced as would be expected if the *o*phen were reduced in this voltage region. This would indicate that the reduction of liberated *o*phen is not a factor in current production at these voltages. This is supported by the fact that there are no similarities between these curves and those for the preceding ions. The addition of gelatin or camphor had no appreciable effect on the shape of curve (d).

IV. CONCLUSION

Of the four complex ions studied, only $[Pt(o\text{phen})_2]^{2+}$ shows evidence for reduction to intermediate compounds. Reduction of the other ions appears to proceed directly to metallic platinum. Adsorption phenomena possibly play an important part in the electrode processes. The initial reduction to metallic platinum is followed by current producing reactions of obscure origin.

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THE STRETCHING FREQUENCY OF THE AZO-GROUP IN FORMAZANS

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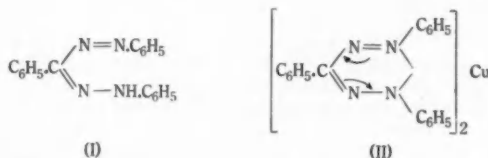
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Summary

Infra-red spectra between 680 and 1600 cm^{-1} are recorded for 10 formazans and five copper complexes derived therefrom. A common feature at c. 1450 cm^{-1} in the formazans is removed by chelation; it is therefore suggested that 1450 cm^{-1} is the stretching frequency of $-\text{N}:\text{N}-$ as modified by conjugation and hydrogen-bonding in a system $\text{Ar.N:N.CAr:N}-$. Analogies with keto-enol systems indicate that azo-groups in simpler environments would absorb at higher frequencies, so that of the two alternatives left open by Le Fèvre, O'Dwyer, and Werner (1953), namely, 1579 or 1406 cm^{-1} , the larger is to be preferred.

I. INTRODUCTION

Le Fèvre, O'Dwyer, and Werner (1953) have reported infra-red spectra over the rock-salt region for 43 substances believed to contain the azo-group; they inferred that $-\text{N}=\text{N}-$ stretching modes—if active in absorption—may have contributed to either or both of the common bands noted at c. 1400 cm^{-1} and c. 1580 cm^{-1} . In view of the indefiniteness of this conclusion measurements have now been made on a number of derivatives of triphenylformazan (I) and



their related copper complexes (II), it being hoped that any band or bands due to the azo-group, in structures based on I, would become modified by resonance in the corresponding chelates II, and be thus detectable.

II. EXPERIMENTAL

(a) Materials

The formazans have been prepared by the methods described by Ashley *et al.* (1953) and the copper chelates by those given by Hunter and Roberts (1941). The m.p.'s and other physical properties agreed with those recorded by these authors.

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(b) *Methods*

The formazans and their copper derivatives have been examined as "Nujol" mulls in the double-beam recording infra-red spectrometer built by one of us (R.L.W.).

Results are presented in Tables 1 and 2, intensities (relative to the strongest absorptions in a given spectrum) being indicated as strong (s), medium (m), and weak (w). The assignments suggested are discussed later.

TABLE 1
SPECTRA OF FORMAZANS AND THEIR COPPER DERIVATIVES

Formazan	Copper Complex	Assignments
1,3,5-Triphenylformazan		
1600 (m)	1602 (w)	1625-1575 benzene band
1582 (w)	1591 (w)	1600-1560 benzene band
1512 (s)	1514 (w)	1500 benzene band
1496 (s)	1498 (w)	1500 benzene band
—	1484 (w)	
1445 (s)	—	—N=N— lowered by hydrogen bonding
—	1408 (v.w.)	
1351 (s)	1354 (m)	
1312 (m)	1327 (m)	C—N
—	1308 (m)	
—	1297 (m)	
—	1250 (s)	Resonance splitting of —N=N— in chelates
1234 (s)	1237 (s)	C—N
1184 (m)	1186 (s)	
1162 (m)	1158 (s)	
1147 (w)	—	C—N
1072 (w)	1076 (m)	Monosubstituted phenyl
1043 (w)	1044 (w)	Monosubstituted phenyl
1019 (w)	1023 (m)	Monosubstituted phenyl
—	998 (m)	
—	987 (m)	
914 (w)	915 (w)	
—	908 (w)	
889 (w)	882 (w)	
—	806 (w)	
763 (m)	—	—CH out of plane
753 (s)	753 (s)	—CH out of plane
740 (m)	—	—CH out of plane
691 (m)	688 (s)	—CH out of plane
—	677 (s)	
1- <i>p</i> -Chlorophenyl-3- <i>p</i> -methoxyphenylformazan		
1608 (m)	1612 (w)	1625-1575 <i>p</i> -substituted benzene band
1599 (m)	—	1625-1575 <i>p</i> -substituted benzene band
—	1585 (w)	1625-1575 benzene band

TABLE I (Continued)

Formazan	Copper Complex	Assignments
<i>1-p-Chlorophenyl-3-p-methoxyphenylformazan (Continued)</i>		
1562 (w)	—	1600-1560 benzene band
1515 (s)	1514 (m)	1500 benzene band
1499 (s)	—	1500 benzene band
1482 (s)	1482 (s)	—
1456 (s)	—	—N=N— lowered by hydrogen bonding
1407 (m)	1409 (m)	—
1357 (m)	1328 (w)	C—N
1300 (w)	1300 (w)	—
1279 (w)	1279 (m)	—
—	1250 (s)	—N=N— resonance splitting in chelates
1246 (s)	1238 (s)	C—N
1223 (s)	1223 (s)	—
1181 (m)	1181 (s)	—
1171 (s)	—	—
—	1152 (s)	C—N
1145 (m)	—	C—N
—	1111 (w)	<i>p</i> -Substituted benzene
1086 (w)	1089 (m)	<i>p</i> -Substituted benzene
1039 (m)	1031 (m)	<i>p</i> -Substituted benzene
1026 (m)	—	<i>p</i> -Substituted benzene
1006 (m)	1008 (w)	<i>p</i> -Methoxyphenyl
—	884 (w)	—
834 (s)	824 (m)	$\nu_4 \perp \text{H}$ of <i>p</i> -substituted benzene
813 (w)	—	—
—	781 (w)	—
768 (m)	761 (w)	$\nu_4 \perp \text{H}$ of monosubstituted benzene
755 (m)	—	$\nu_4 \perp \text{H}$ of monosubstituted benzene
733 (m)	—	$\nu_4 \perp \text{H}$ of monosubstituted benzene
721 (m)	—	$\nu_4 \perp \text{H}$ of monosubstituted benzene
690 (m)	694 (w)	$\nu_4 \perp \text{H}$ of monosubstituted benzene
<i>1-p-Chlorophenyl-3,5-diphenylformazan</i>		
1600 (m)	1602 (w)	1625-1575 <i>p</i> -disubstituted benzene band
1588 (w)	1585 (w)	1600-1560 benzene band
1514 (s)	1499 (w)	1500 benzene band
1491 (s)	1481 (m)	1500 benzene band
1448 (s)	—	—N=N— lowered by hydrogen bonding
1407 (m)	1411 (w)	—
1353 (m)	1345 (w)	—
1320 (w)	1320 (w)	C—N
—	1309 (w)	—
—	1297 (m)	—
—	1282 (m)	—
—	1268 (m)	—
—	1251 (s)	Resonance splitting of —N=N—
1234 (s)	1236 (s)	C—N

TABLE 1 (Continued)

Formazan	Copper Complex	Assignments
<i>1-p-Chlorophenyl-3,5-diphenylformazan (Continued)</i>		
1179 (m)	1183 (s)	C—N <i>p</i> -Disubstituted benzene <i>p</i> -Disubstituted benzene <i>p</i> -Disubstituted benzene
—	1154 (s)	
—	1103 (w)	
1098 (m)	—	
1084 (m)	1089 (m)	Monosubstituted benzene
1071 (w)	1078 (w)	Monosubstituted benzene
1044 (m)	1057 (w)	Monosubstituted benzene
—	1026 (w)	Monosubstituted benzene
1018 (w)	1015 (w)	Monosubstituted benzene
—	984 (w)	$\nu_4 \perp H$ <i>p</i> -Disubstituted benzene $\nu_4 \perp H$ <i>p</i> -Disubstituted benzene $\nu_4 \perp H$ <i>p</i> -Disubstituted benzene $\nu_4 \perp H$ Monosubstituted benzene
836 (m)	—	
827 (m)	825 (w)	
809 (m)	809 (w)	
765 (s)	—	$\nu_4 \perp H$ Monosubstituted benzene
757 (s)	758 (m)	$\nu_4 \perp H$ Monosubstituted benzene
692 (s)	694 (w)	$\nu_4 \perp H$ Monosubstituted benzene
—	688 (m)	$\nu_4 \perp H$ Monosubstituted benzene
—	677 (m)	$\nu_4 \perp H$ Monosubstituted benzene
<i>1-p-Bromophenyl-3-p-methoxyphenyl-5-phenylformazan</i>		
1605 (m)	1610 (m)	1625–1575 <i>p</i> -substituted benzene band
1600 (m)	1604 (w)	1625–1575 monosubstituted benzene band
1590 (m)	1594 (w)	1600–1560 benzene band
—	1585 (w)	—
1575 (w)	—	1500 benzene band 1500 benzene band 1500 benzene band
1514 (s)	1516 (s)	
—	1494 (w)	
1485 (s)	—	—N=N— lowered by hydrogen bonding
1461 (s)	—	
1453 (s)	—	
1395 (m)	1404 (w)	C—N <i>p</i> -Methoxyphenyl —N=N— resonance split by chelation
1355 (m)	1357 (w)	
1300 (w)	1300 (w)	
1247 (s)	1247 (s)	C—N
—	1238 (s)	C—N
1227 (s)	1227 (s)	C—N
—	1183 (s)	C—N C—N <i>p</i> -Disubstituted benzene
1172 (m)	1172 (s)	
—	1152 (m)	
1145 (m)	—	<i>p</i> -Disubstituted benzene
—	1108 (w)	<i>p</i> -Disubstituted benzene
1086 (w)	1097 (w)	Monosubstituted benzene
—	1069 (m)	

TABLE 1 (Continued)

Formazan	Copper Complex	Assignments
1- <i>p</i> -Bromophenyl-3- <i>p</i> -methoxyphenyl-5-phenylformazan (Continued)		
1044 (w)	—	Monosubstituted benzene
1028 (m)	1026 (m)	Monosubstituted benzene
1003 (w)	1006 (w)	<i>p</i> -Methoxyphenyl
828 (s)	832 (m)	$\nu_4 \perp H$ <i>p</i> -Disubstituted benzene
—	823 (m)	$\nu_4 \perp H$ <i>p</i> -Disubstituted benzene
804 (m)	—	$\nu_4 \perp H$ <i>p</i> -Disubstituted benzene
—	782 (w)	
769 (m)	768 (w)	$\nu_4 \perp H$ Monosubstituted benzene
684 (m)	688 (w)	$\nu_4 \perp H$ Monosubstituted benzene
1,5-Diphenyl-3- <i>p</i> -methoxyphenylformazan		
1610 (m)	1610 (w)	1625–1575 <i>p</i> -substituted benzene band
1601 (m)	—	1600–1560 benzene band
1583 (m)	1584 (w)	1600–1560 benzene band
1515 (s)	1514 (m)	1500 benzene band
1501 (s)	—	1500 benzene band
1456 (s)	—	—N=N— lowered by hydrogen bonding
1400 (w)	—	
1361 (m)	—	
1314 (m)	1322 (m)	C—N
1301 (m)	1304 (m)	
1248 (s)	1248 (s)	<i>p</i> -Methoxyphenyl
—	1240 (s)	Resonance splitting of —N=N— in chelates
1230 (s)	1238 (s)	C—N
1185 (m)	—	
1175 (s)	1172 (s)	
1165 (m)	—	
1153 (m)	1151 (s)	C—N
1146 (m)	—	
—	1110 (w)	<i>p</i> -Substituted phenyl
1076 (w)	1075 (w)	Monosubstituted phenyl
1045 (m)	—	Monosubstituted phenyl
1028 (s)	1029 (m)	Monosubstituted phenyl
1007 (m)	1007 (w)	<i>p</i> -Methoxyphenyl
—	997 (w)	
—	983 (w)	
843 (m)	843 (w)	
839 (m)	832 (m)	$\nu_4 \perp H$ <i>p</i> -Substituted phenyl
820 (m)	819 (w)	$\nu_4 \perp H$ <i>p</i> -Substituted phenyl
—	780 (w)	$\nu_4 \perp H$ Monosubstituted phenyl
770 (s)	769 (w)	$\nu_4 \perp H$ Monosubstituted phenyl
757 (m)	759 (w)	$\nu_4 \perp H$ Monosubstituted phenyl
721 (m)	—	$\nu_4 \perp H$ Monosubstituted phenyl
687 (m)	691 (w)	$\nu_4 \perp H$ Monosubstituted phenyl
—	667 (w)	$\nu_4 \perp H$ Monosubstituted phenyl

Since the formazans appeared all to absorb near 1450 cm^{-1} , and because such a point is close to the 1464 cm^{-1} maximum recorded for the "Nujol" used, the spectra were repeated between 1400 and 1480 cm^{-1} with hexachlorobutadiene

TABLE 2
SPECTRA OF FIVE FORMAZANS

A*	B*	C*	D*	E*	Assignments
1598 (m)	1599 (s)	1598 (s)	1594 (s)	1594 (s)	1625-1575 cm^{-1} band of benzene
1582 (m)	1582 (m)	1585 (m)	1582 (s)	1576 (m)	1625-1575 cm^{-1} band of benzene
1575 (w)	—	—	1570 (m)	1563 (m)	1600-1560 band of benzene
1508 (s)	1518 (s)	1514 (s)	1512 (s)	—	1500 band of benzene
1503 (s)	1504 (s)	—	1503 (s)	1504 (s)	1500 band of benzene
1485 (s)	—	1498 (s)	1496 (s)	—	1500 band of benzene
1442 (s)	1445 (s)	1443 (s)	1445 (s)	1444 (s)	—N=N— lowered by hydrogen bonding
1403 (m)	1426 (m)	1426 (m)	1404 (m)	1409 (m)	
1351 (m)	1365 (m)	—	1329 (s)	—	C—N
—	1323 (s)	—	—	1323 (s)	—N—O symmetrical stretching
—	—	—	1314 (s)	—	
—	—	1292 (m)	—	1298 (m)	
—	—	1247 (s)	—	—	<i>p</i> -Methoxyphenyl
1231 (s)	1222 (s)	1228 (s)	1217 (s)	1221 (s)	C—N
1184 (m)	—	1181 (m)	—	—	
1165 (m)	1165 (m)	—	1165 (m)	1165 (m)	C—N
1150 (m)	—	—	—	—	
—	—	1141 (m)	—	1145 (m)	
—	1109 (s)	—	1106 (s)	1106 (s)	
—	—	—	1098 (s)	1098 (s)	
—	—	—	1108 (w)	1086 (w)	<i>p</i> -Substituted phenyl
1062 (m)	—	—	1065 (s)	—	
1041 (m)	—	1034 (m)	1035 (m)	1035 (m)	<i>p</i> -Substituted phenyl
1017 (m)	1013 (m)	1018 (m)	1014 (m)	1016 (m)	<i>p</i> -Substituted phenyl
1006 (m)	—	—	1006 (m)	—	
—	—	—	999 (m)	—	
—	847 (m)	—	848 (m)	—	$\nu_4 \perp \text{H}$ of <i>p</i> -disubstituted benzene
827 (m)	—	833 (m)	830 (s)	837 (s)	$\nu_4 \perp \text{H}$ of <i>p</i> -disubstituted benzene
816 (m)	—	—	—	813 (w)	$\nu_4 \perp \text{H}$ of <i>p</i> -disubstituted benzene
805 (m)	—	—	—	—	$\nu_4 \perp \text{H}$ of <i>p</i> -disubstituted benzene
763 (s)	758 (m)	767 (w)	767 (m)	770 (m)	$\nu_4 \perp \text{H}$ of monosubstituted benzene
—	750 (s)	752 (w)	751 (m)	751 (m)	$\nu_4 \perp \text{H}$ of monosubstituted benzene
692 (s)	683 (m)	692 (s)	692 (s)	692 (m)	$\nu_4 \perp \text{H}$ of monosubstituted benzene

* Key to substances: A. 1-*p*-Bromophenyl-3,5-diphenylformazan. B. 1-*p*-Nitrophenyl-3,5-diphenylformazan. C. 1-*p*-Methoxyphenyl-3,5-diphenylformazan. D. 1,3-Di-(*p*-methoxyphenyl)-5-phenylformazan. E. 1-*p*-Chlorophenyl-3-phenyl-5-nitrophenylformazan.

(which is practically transparent at 1450 cm^{-1}) as the mulling agent. Table 3 shows the peaks observed; the copper derivatives are not listed specifically because with them absorptions c. 1450 cm^{-1} were either absent or very feeble.

TABLE 3

ABSORPTIONS NEAR 1450 cm^{-1} OF FORMAZANS MULLED WITH HEXACHLORO-BUTADIENE

Formazan	Absorption Maximum Observed (cm^{-1})
Triphenyl-	1447
1- <i>p</i> -Chlorophenyl-3,5-diphenyl-	1449
1- <i>p</i> -Chlorophenyl-3-phenyl-5-nitrophenyl-	1447
1- <i>p</i> -Bromophenyl-3,5-diphenyl-	1444
1- <i>p</i> -Methoxyphenyl-3,5-diphenyl-	1445
1,3-Di- <i>p</i> -methoxyphenyl-5-phenyl-	1445
1,5-Diphenyl-3- <i>p</i> -methoxyphenyl	1457
1- <i>p</i> -Chlorophenyl-3- <i>p</i> -methoxyphenyl-5-phenyl-	1457
1- <i>p</i> -Bromophenyl-3- <i>p</i> -methoxyphenyl-5-phenyl-	1458
1- <i>p</i> -Nitrophenyl-3,5-diphenyl-	1447

III. DISCUSSION

A survey of Tables 1 and 2 shows that the formazans and their copper derivatives have common frequencies in seven regions. These however may be easily assigned:

Region (cm^{-1})	Assignment
1594 to 1612 } 1576 to 1601 } 1498 to 1518 }	"Benzene" bands
1221 to 1238	C-N
1013 to 1031	Substituted phenyl
753 to 770 } 683 to 694 }	C-H (out of plane)

Medium or weak absorption is observed in all the formazans (except triphenyl-formazan) at about 1400 cm^{-1} , so that at first glance the present results harmonize with those (viz. absorptions at c. 1580 and 1400 cm^{-1}) of Le Fèvre, O'Dwyer, and Werner (1953) for azobenzene and various other azo-compounds. However, since similar frequencies occur in some of the copper chelates, their connection with the $-\text{N}=\text{N}-$ group can be discounted.

By the last criterion the features between 1442 and 1456 cm^{-1} in the formazans become significant, because although clear in the parent substances they either disappear or are very much weakened in the metallic complexes. The question thus arises: may absorption at c. 1450 cm^{-1} be connected with the double-bonded nitrogen unit?

An affirmative answer seems possible by analogy with certain keto-enol systems. Structures of type I, in which the aryl radicals are disposed in a *trans*-sense about the $\text{N}=\text{N}$ group, show "virtual tautomerism" through

possession of internal H bonds (cf. Hunter and Roberts 1941). Now whereas *inter*-molecular H bonding shifts the stretching frequency of C=O by 10 cm^{-1} (Grove and Willis 1951), *intra*-molecular H bonding of the mesomeric kind found with keto-enols causes much larger modifications. Flett (1948) noted that $\nu_{\text{C=O}}$ in 1-hydroxyanthraquinone was abnormally low; clear examples of the same effect were provided by Rasmussen, Tunnicliffe, and Brattain (1949) with β -diketones such as acetylacetone. Other relevant observations have been made by Hunsberger (1950), Hunsberger, Ketcham, and Gutowsky (1952), Leonard *et al.* (1952), Park, Brown, and Lacher (1953), and Bellamy and Beecher (1954), all of which indicate that "conjugate chelation" produces a $\nu_{\text{C=O}}$ which is 70 to 100 cm^{-1} below the "normal" figure of about 1700 cm^{-1} . Various tropolones exhibit ketonic frequencies between 1610 and 1630 cm^{-1} (cf. Le Fèvre, Maramba, and Werner 1953).

It is therefore suggested that the absorption around 1450 cm^{-1} is in fact the $\nu_{\text{N=N}}^*$ appropriate in a system Ar.N:N.CAr.N- shifted to longer wavelengths by internal hydrogen bonding.

With keto-enolic compounds, the formation of metallic chelates leads to more complete resonance between the contributing structures and the C=O and C—O links, both assume an intermediate double-single bond character, usually detected by the appearance of two bands whose intensities are similar (Morgan 1949; Duval, Lecomte, and Freymann 1950, 1952; Lecomte 1950; Bellamy, Spicer, and Strickland, 1952; Bellamy and Branch 1954) although if resonance is incomplete only a single frequency may be observed (e.g. with salicylaldehyde complexes, Bellamy and Branch 1954).

Some parallels with the last remarks may be discerned among the spectra of the present paper. Thus the formation of copper complexes from the formazans is attended by certain characteristic changes in the absorption pattern: the number of frequencies displayed in the 1300 cm^{-1} region is increased and a strong band appears near 1250 cm^{-1} . These may be attributed to "resonance splitting". This interpretation implies changes in N—H and C=N frequencies; we intend to consider these at a later date when a wider range of experimental evidence is available.

IV. CONCLUSIONS

(i) Evidence now available makes the assignment of 1450 cm^{-1} as a stretching frequency of —N=N— modified by conjugation and hydrogen-bonding not unlikely.

(ii) Since with the C=O group conjugation and hydrogen-bonding operate to shift $\nu_{\text{C=O}}$ towards longer wavelengths, by analogy the frequency appropriate for an unmodified —N=N— linkage should be higher, not lower, than 1450 cm^{-1} . Therefore, of the two alternatives left open by Le Fèvre, O'Dwyer, and Werner (*viz.* 1406 or 1579 cm^{-1}) for the azo-group, the lower can now be rejected. Such a choice agrees with that made by Herzberg (1945).

* $\nu_{\text{N=N}}$ in this system will in any case be less than 1580 cm^{-1} suggested for $\nu_{\text{N=N}}$ in a monoazo-compound as a result of conjugation.

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MIGRATION OF EXCITATION ENERGY IN ORGANIC CRYSTALS

I. TETRACENE INCLUDED IN ANTHRACENE

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Summary

The fluorescence spectra excited from anthracene crystals containing traces of tetracene have been accurately recorded using a spectrometer with a photomultiplier as detector. In addition polarized fluorescence spectra from very thin anthracene single crystals have been reported. From the results it is concluded that energy migration from anthracene to tetracene is by a non-radiative mechanism, although it is shown that reabsorption of fluorescence can significantly modify the characteristics of such crystals. In addition, it is shown that this system has a limit of solid solution for crystals grown by sublimation (about 10^{-2} mole/mole) above which the characteristics are markedly altered because of the formation of minute tetracene crystals.

I. INTRODUCTION

Since the pioneer studies of the depolarization of fluorescence by Gaviola and Pringsheim (1924) evidence from many fields has confirmed that interaction occurs between electronically excited molecules and neighbouring unexcited ones. An example of prime importance occurs in the photosynthetic process; however, problems of technique have, until recently, limited quantitative study in this complicated field.

Much work remains to be done to complete our knowledge of the quantitative characteristics of the energy transfer associated with this special type of interaction. The present paper describes quantitative results obtained with an example of an important type of system, namely tetracene included in small concentrations in anthracene crystals. This and analogous examples of host-impurity transfer have been discussed previously in a number of publications (Bowen, Mikiewicz, and Smith 1947, 1949; Lipsett and Dekker 1952; Schmitten 1953; Schmitten, Schmitten, and Rohde 1953); the present work however is directed to aspects such as the effects of crystal thickness and concentration of impurity, hitherto insufficiently studied.

II. EXPERIMENTAL

(a) Apparatus

The fluorescence spectra were measured with two spectrometers both modified to some extent. The first was a constant-deviation Hilger D186 instrument with a 1P21 photomultiplier fitted as a detector. The second was a Beckman DU spectrophotometer in which the phototube housing and cell block

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were replaced by a box containing a 1P28 photomultiplier. The voltage supply was provided by a stack of "Minimax" batteries and the photocurrent amplified as previously described (Ferguson, Iredale, and Taylor 1954).

An optical bench was used with the Beckman placed at right angles to the entrance mirror. The lenses, a Wollaston prism, and crystal holder were mounted on it. The Wollaston was mounted in one unit with two lenses, one in front, the other behind, so that the two plane-polarized images appeared one above the other. A 180° rotation could be made to invert the position of the two images. The Beckman favoured radiation polarized in a vertical plane slightly more than that polarized horizontally and a correction factor was determined and used.

Calibration of the constant-deviation unit has been described (Ferguson, Iredale, and Taylor 1954) and a similar procedure was followed with the Beckman unit.

The Beckman with photomultiplier attachment was used both for measuring fluorescence spectra from single anthracene crystals and also to study the variation of fluorescence efficiency with the wavelength of the exciting radiation in the anthracene-tetracene crystals. For the latter, the crystals, grown between silica disks, were placed in front of the photocathode with all except a pin-hole blocked out by a shield. Light from a calibrated tungsten lamp was passed into the Beckman and the response of the photomultiplier recorded at different wavelengths between 3200 and 4000 Å, with constant slit and the Beckman optical filter in the light path. The photomultiplier thus recorded the relative intensity of the fluorescence as a function of the wavelength of the exciting radiation.

The fluorescence spectra were excited with 3650 Å radiation from a Philips 125 W mercury "black" lamp with an additional Corning 7-54 filter.

(b) Purification of Materials

Anthracene was purified by chromatography on alumina in light petroleum (60–90 °C) as solvent. Exclusion of light in the presence of oxygen is essential to prevent photo-oxidation of the anthracene to anthraquinone on the column. Single crystals were prepared by sublimation in an atmosphere of carbon dioxide.

The tetracene (naphthacene), a Light's undesignated sample, was recrystallized from xylene in the dark under nitrogen.

(c) Preparation of the Anthracene-Tetracene Crystals

Approximately 2 g of a mixture containing 10^{-3} mole of tetracene per mole of anthracene was made. This was sealed-off under nitrogen and melted in an oil-bath at about 240 °C and then cooled quickly. Other mixtures were made from this by a similar procedure having the following mole ratios: 10^{-4} , 3×10^{-5} , 10^{-5} , and 2×10^{-6} .

For low mole ratios of tetracene a small amount of the mixture was just melted between silica disks on an electrical hot-plate. This was then taken off the hot-plate so that the melt quickly crystallized to form a very thin layer between the disks. Other methods of sample preparation were tried, but the

ideal sample crystal must present the minimum optical path for the escape of fluorescence and this method gave the best crystals. All apparatus was checked for traces of impurity with a black lamp.

Crystals containing more than one molecule per thousand of tetracene were grown by sublimation in an atmosphere of carbon dioxide. It was not found possible in this way to grow crystals of predetermined concentration but two crystals, brown in colour, were found, from their absorption spectra when dissolved in benzene, to have mole ratios of about 8×10^{-3} . These crystals (see Section III) are beyond the solid solution limit and, although apparently single when viewed through the polarizing microscope, consist of layers of tetracene interleaved in the anthracene matrix.

III. RESULTS

(a) Anthracene Crystal Fluorescence

The polarized fluorescence spectrum of anthracene crystal, measured from two crystals is included (Figs. 1 and 2). The thicknesses of the crystals (sublimation flakes) are not accurately known but the thicker was probably about 1μ , with the thinner about 0.5μ .

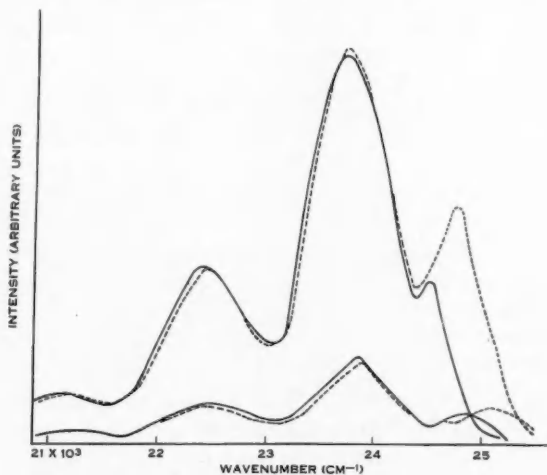


Fig. 1.—Fluorescence spectrum from a thin single anthracene crystal recorded in *a* and *b* polarizations with front and back face illumination. The broken curve shows the front face illumination, the lower curve in each case being *a* polarized. The effect of reabsorption is obvious.

(b) Anthracene-Tetracene Crystals

Figure 3 records the relative intensities emitted by anthracene and tetracene for crystals having the following mole ratios: 2×10^{-6} , 10^{-5} , 3×10^{-5} , and 10^{-4} respectively. The spectral intensity is plotted against wavenumber in each case and the peak wavenumbers of the fluorescence are given in Table 1.

It was not possible with the constant-deviation spectrometer to measure below about $24,000\text{ cm}^{-1}$. For this reason the anthracene emission is shown in this region by a broken line, uncorrected for reabsorption. All the curves could be accurately reproduced and were repeated several times with different samples.

It is evident from these diagrams that there is a remarkable change in character of the emission as the concentration of tetracene is increased, and at a mole ratio of 10^{-4} only a very small fraction of the light comes from the anthracene. The uncertainty in the dotted portions of the spectra makes it impossible to determine the ratio of anthracene to tetracene fluorescence at

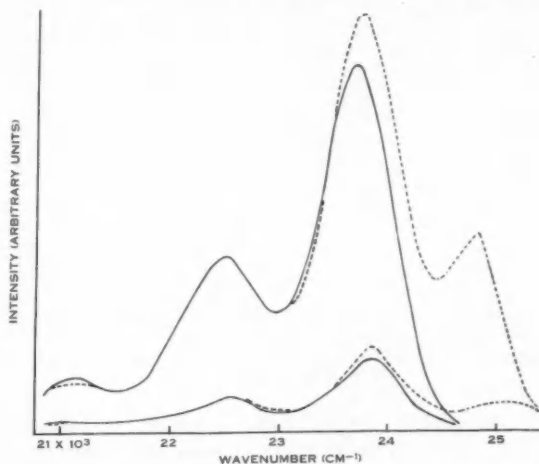


Fig. 2.—Fluorescence spectrum from a thin single anthracene crystal (thickness about 1μ), plotted as in Figure 1. All trace of the 4000 \AA band has been lost in both polarizations with back face illumination.

each concentration (ratio of areas under the curves), but a visual estimate is that this ratio is about equal to one at a mole ratio of about 10^{-5} , implying that at this concentration one-half of the emitted energy comes from the tetracene. This is the same order as that found by Bowen, Mikiewicz, and Smith (1947) from quantum yield measurements.

No sufficiently accurate method of measurement of crystal thickness was available, but the crystals were thin enough to prevent serious reabsorption of the tetracene fluorescence since no reabsorption could be detected even at a mole ratio of 10^{-4} . A simple calculation shows that if 10 per cent. reabsorption can be tolerated for the highest energy emission band of tetracene then 0.2 mm is the maximum permissible thickness for the crystal sample. All the crystals were thinner than this. Another check of the crystal thickness, or more important, the path traversed by the fluorescence, is obtained from a comparison of the anthracene band positions with those obtained from the single anthracene

crystals shown in Figures 1 and 2. The band reported at $23,650\text{ cm}^{-1}$, in Table 1, is removed by 150 cm^{-1} from the corresponding band in Figure 1 and only by 100 cm^{-1} from that in Figure 2. The thickness of the latter crystal was

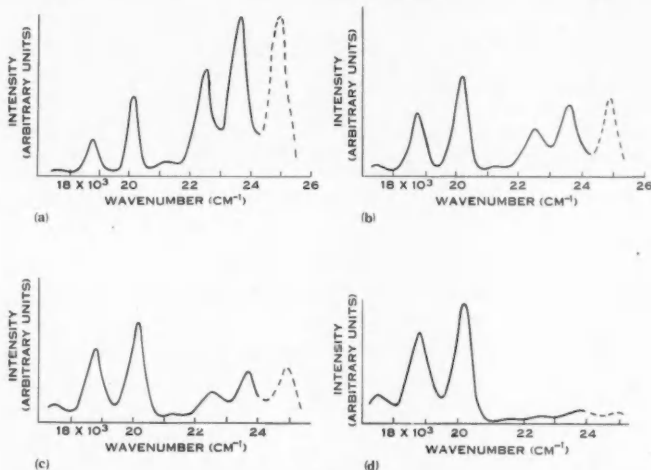


Fig. 3.—Fluorescence spectra excited from thin anthracene-tetracene crystals having mole ratios: (a) 2×10^{-6} , (b) 10^{-5} , (c) 3×10^{-5} , and (d) 10^{-4} . The broken curves show peaks outside the limit of measurement, uncorrected for reabsorption.

known to be of the order 0.001 mm from measurements with the polarizing microscope, so that it is probable that the crystals used were not much thicker than this because of the closeness of the band positions.

TABLE I
PEAK POSITIONS IN THE FLUORESCENCE SPECTRUM OF ANTHRACENE-TETRACENE CRYSTALS

Compound						Peak Position (cm^{-1})
Anthracene	$23,650 \pm 150$
						$22,500 \pm 50$
						$21,100 \pm 50$
Tetracene	$20,200 \pm 50$
						$18,800 \pm 50$
						$17,450 \pm 50$

It is often assumed that the results for a sample consisting of a polycrystalline mass are the same or, at least, nearly the same as those for a single crystal. This is not true and is the cause of confusion in the literature. The results for such a

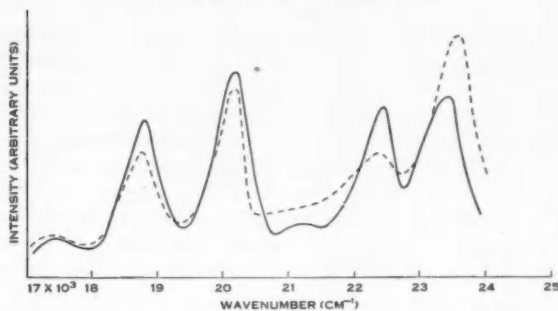


Fig. 4.—The full line records the fluorescence spectrum at room temperature from a solution of mole ratio 10^{-5} and the broken line that obtained at -180°C without moving the sample.

polycrystalline sample are shown in Figure 4. The crystals were ground between silica disks and placed in a low temperature absorption cell. The low temperature reduces the amount of overlap between absorption and fluorescence spectra,

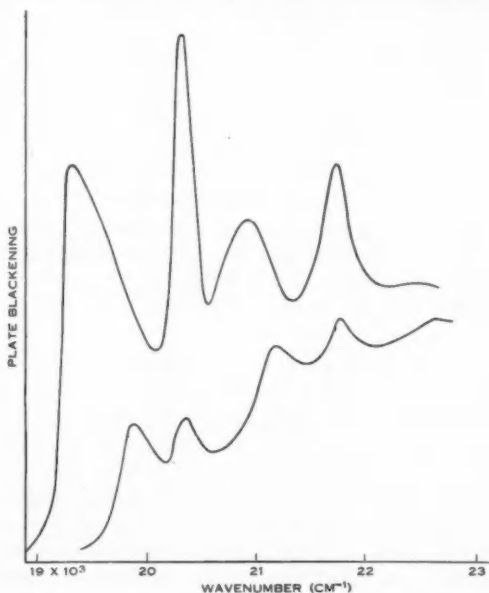


Fig. 5.—Absorption spectrum (microphotometer tracing) of a single mixed crystal of mole ratio about 8×10^{-5} at -180°C . The upper curve represents the absorption parallel to the b crystal axis and the lower parallel to the a crystal axis. (Tetracene solution bands at $20,300$ and $23,800\text{ cm}^{-1}$ in both polarizations.)

hence the amount of reabsorption, so that the emission approximates to the spectrum of the thin crystal, except for the presence of scattered background radiation.

There is an upper limit to the concentration of foreign molecules which can be tolerated in a crystal before the structure is seriously altered. In general, at greater concentrations the impurity molecules tend to coalesce within the structure and to form layers consisting solely of the impurity between layers of the mixture of parent and foreign molecules. Crystals, in which this upper limit has been exceeded, are difficult to detect by microscopy, and some erroneous conclusions have been reported from the failure to realize that crystals of mixed

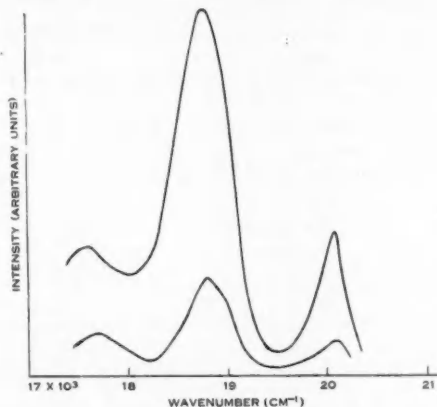


Fig. 6.—Fluorescence spectrum at -180°C from the crystal of which the absorption spectrum is shown in Figure 5. The upper curve is that polarized parallel to the b crystal axis and the lower parallel to the a crystal axis.

hydrocarbons can contain these zones of impurity crystals in addition to the true solid solution. This is strikingly demonstrated in Figure 5 which shows a microphotometer tracing of the absorption of polarized light by a crystal containing tetracene at a mole ratio of about 8×10^{-3} (at -180°C). This spectrum contains not only the absorption spectrum of tetracene in true solid solution (band peaks at 4585 and 4925 Å), but also that of pure tetracene crystals which are apparently present in zones or layers in the matrix and show strong pleochroic absorption (Bree and Lyons 1954). Figure 6 shows the fluorescence (at -180°C) of the crystal of which the absorption spectrum is shown in Figure 5. As can be seen the intensity of the $20,200\text{ cm}^{-1}$ peak is considerably lower relative to the $18,000\text{ cm}^{-1}$ peak (compare with Fig. 3) because of the tetracene crystal absorption between 5000 and 5200 Å.

In order to examine the fluorescence efficiency as a function of the wavelength of the exciting radiation, the modified Beckman described in Section II was used and the relative intensity of the fluorescence measured. It is possible

to calculate the relative energy distribution of the light incident on the crystal using data on the relative dispersion of the Beckman and the optical transmission of its filter, so the variation of fluorescence efficiency with wavelength can be deduced. The comparison of the observed and calculated relative distributions for all crystals used showed that the fluorescence yield is independent of the wavelength of the exciting radiation between 3200 and 4000 Å.

IV. DISCUSSION

Birks (1954) has recently claimed that energy migration phenomena, including the example discussed here, can be explained by a simple photon mechanism, that is, a series of steps in which the light, originally absorbed by one molecule is transferred to other molecules by emission and absorption. Although these steps will be shown to be unimportant when applied to the transfer process, they introduce significant modifications to the fluorescence characteristics of crystals when the series of steps involve molecules of the same species.

The application of the mechanism to the transfer process will be considered first. The steps can be represented by the following simplified system of equations:



in which the A's and T's refer to molecules of anthracene and tetracene respectively; an asterisk denotes an excited molecule and ν is the frequency emitted or absorbed by the molecules. In these equations it is understood that energy changes other than the pure electronic take place; T^* in step (3), for example, will in general have energy in excess of that possessed by T^* in step (4), because of the possible excitation of vibrations in the former case. Absence of quenching is also assumed.

The efficiency of the photon mechanism depends on the extent to which step (3) operates, in other words, on the fraction of the total number of quanta $h\nu_A$, absorbed by the tetracene molecules in the sample. This fraction will be determined by the absorption coefficient of tetracene, the density of the molecules in the sample, and the path length traversed by the fluorescence through the sample. Although it becomes a difficult problem to calculate the fraction of the total energy absorbed by the tetracene molecules (because the absorption coefficient is a varying function of the frequency and also because of a similar variation in step (2)) calculations at particular frequencies can be made as well as deductions concerning the consequences to be expected from its operation.

In the latter case, if the fluorescence spectrum of anthracene crystal is superposed on the absorption spectrum of tetracene dissolved in anthracene, then it is seen that absorption of the anthracene fluorescence by the tetracene will be relatively greater at the minima of the anthracene fluorescence spectrum



than elsewhere and, of course, absorption will not be constant over the whole of the spectrum. The effect will be to make the anthracene fluorescence maxima stand out sharply from the minima, and also it will alter the relative intensity of the peaks in different mixtures. As can be seen from Figure 3, both these effects are absent.

As an example of the former case, the upper limit of the thickness of a crystal in which 50 per cent. of the anthracene fluorescence (all assumed to traverse the thickness of the crystal) at the $23,800\text{ cm}^{-1}$ peak is absorbed by the tetracene (extinction coefficient about 3000), for a molar concentration of 6×10^{-5} (corresponding to a mole ratio of 10^{-5}) is found simply to be 16 mm.

This thickness is very much greater than that of any crystal used. A photon mechanism is thus unable to explain the observation that a very thin crystal of this concentration emits about one-half of the fluorescence energy from the tetracene when excitation occurs in the anthracene.

The same conclusion can be reached another way: the crystals were so thin that the tetracene could just be detected photographically at a mole ratio of the order 10^{-3} , so even at this relatively high concentration the capture of anthracene fluorescence by photon absorption is negligible.

The failure of a radiative mechanism, at least in the example treated here, leaves as the probable mechanism that of resonance transfer used so successfully by Förster (1947, 1949a, 1949b) for dye solutions. This transfer is a consequence of the forces of interaction between excited and unexcited molecules, and for the cases of most interest these are adequately described in the dipole-dipole approximation as resonance forces which fall off as the inverse 4th power of the intermolecular distance. The importance of these forces in the theory of molecular crystal spectra has been pointed out by Craig and Hobbins (1955), and as mentioned by them, the exchange of excitation between the *molecules* of a *crystal lattice* is formally analogous to the motion of a spinless particle which has been called the exciton.

The close proximity of the anthracene and tetracene molecules (nearest neighbours in the crystal lattice) prevents the use of perturbation theory for calculation of the transfer probability and only the general features of the mechanism can be deduced. Change of temperature (to -180°C) has no detectable effect on the efficiency, so the loss of energy, in excess of that emitted by the tetracene molecules, must take place very quickly compared with the fluorescence lifetime. Loss of energy, in excess of that corresponding to the lowest excited electronic state, does in fact take place exceedingly quickly as is shown by the constancy of the fluorescence efficiency with wavelength of the exciting radiation. This shows that no matter the wavelength of the light absorbed by the anthracene, the energy has the same chance of being trapped by a tetracene molecule. Apparently therefore, energy absorbed by the anthracene migrates quickly through the lattice, a type of internal conversion analogous to the molecular case taking place, so that the excess energy is lost to the lattice until the lowest excited crystal state is reached. Presumably at this stage, only because most time would be spent here (fluorescence from

pure anthracene crystal occurs from the lowest level), interaction with the tetracene impurity becomes the dominant effect. Excess energy is again lost to the lattice and the tetracene molecule ends in a low, or zero, vibrational level of its excited electronic state. The reverse step does not occur because the energy difference between the purely electronic excited states of the two molecules (about 5000 cm^{-1}) is much greater than the mean thermal energy per degree of vibrational freedom of the crystal at room temperature (210 cm^{-1}), and the energy remains with the tetracene molecule until radiation takes place.

Although reabsorption of fluorescence is unimportant in the transfer process it has a considerable effect (dependent on the crystal thickness) on the fluorescence characteristics. It influences the relative intensity of the bands, their number and wavelength, and their decay times.

The spectra from the single anthracene crystals (Figs. 1 and 2) illustrate most effectively the consequences of reabsorption. For very thin crystals only the highest energy peak is affected and, as is expected from the absorption spectrum, the effect is greater for the *b* than the *a* polarization.

The only published spectral intensity data for the system anthracene-tetracene are those of Lipsett and Dekker (1952). These workers have however worked with samples of appreciable thickness, as is shown by the variation of relative peak intensities of the tetracene bands, clearly caused by reabsorption. Also the use of X-rays as a means of excitation has introduced similar complications. Under X-ray radiation the excitation of the molecules is not limited to those near the surface of the crystal, as is the case with ultraviolet excitation because of its greater efficiency, but is distributed throughout the depth of the crystal. The fluorescence generated by X-ray excitation will therefore have a longer path to traverse and the reabsorption will be greater as evidenced by their results.

The use of large crystals as scintillation counters by physicists has led to unexplained anomalies in the characteristics of these crystals. For example, Elliot, Liebson, and Ravilious (1950) report a decrease of decay time for anthracene fluorescence as the temperature is lowered. The quantum yield however increases with decrease of temperature (Bowen, Mikiewicz, and Smith 1947) so that the drop in decay time must be an example of the effect of reabsorption on the fluorescence; the drop in temperature decreases the overlap between absorption and fluorescence spectra. Further, Liebson, Bishop, and Elliot (1950) report unexplained differences between the decay times under γ -ray and ultraviolet excitation for a number of scintillators. The decay time is greater in the former case. The explanation lies, as with the work of Lipsett and Dekker above, in the efficiency of the excitor; γ -rays penetrate further into the crystals, the fluorescence has a longer path to traverse, and reabsorption becomes relatively greater resulting in larger decay times.

A further factor affecting only the fluorescence characteristics of mixed crystals is the limit of the solid solution, which has hitherto been neglected. It was found that tetracene is dispersed in anthracene as a true solid solution only when the mole ratio is less than about 10^{-3} in crystals grown by sublimation.

The absorption bands of such crystals, at 4925 and 4585 Å, are characteristic of tetracene in solution and a mirror-image relationship is observed with the fluorescence spectrum. In this range of concentration the bands show none of the characteristic properties of crystalline tetracene; however, when the concentration of tetracene is increased the absorption spectrum becomes complicated by the appearance of new bands (Fig. 5), which may readily be identified as those of tetracene crystal by the use of polarized light. As is known (Bree and Lyons 1954), these bands show "Davydov" splitting, and this splitting is diagnostic for the presence of crystalline tetracene. Between mole ratios of 10^{-3} and 10^{-2} therefore, it may safely be concluded that crystals grown by sublimation have tetracene molecules included not only in solid solution, but also in the form of minute tetracene crystals.

The system anthracene-tetracene is therefore a solid solution only at mole ratios below about 10^{-3} , and above this concentration it has two phases with essentially different electronic properties. The two phases are mutually oriented however, in such a way that the optical properties determined with a polarizing microscope do not reveal their lack of homogeneity, doubtless because of the similarity of the crystal structures of anthracene and tetracene.

It is well known that tetracene crystal fluorescence is very weak; Bowen, Mikiewicz, and Smith (1949) reporting a quantum yield at room temperature of 0.002. Energy trapped by the layers of tetracene crystals in the mixed crystal will therefore be dissipated thermally and the quantum yield will drop as is found (Bowen, Mikiewicz, and Smith 1949). The effect on the fluorescence spectrum is shown in Figure 6, where the intensity of the $20,000\text{ cm}^{-1}$ peak (tetracene in solid solution) has dropped relative to the $18,800\text{ cm}^{-1}$ peak because of the tetracene crystal absorption in this region.

This latter effect on the fluorescence spectrum was found by Schmillen, Schmillen, and Rohde (1953) but was unexplained by them. These workers found also a decrease in decay time of the tetracene emission above mole ratios of 10^{-3} ; this is of course consistent with the strong quenching action by the layers of tetracene crystals and is significant as it shows that it occurs through an interaction between tetracene in solid solution and tetracene crystal resulting in a further transfer of energy.

In conclusion it may be stated that energy migration in the system studied here is successfully interpreted by a non-radiative mechanism involving the interaction of electronically excited molecules and unexcited ones. However, in order to interpret the characteristics fully, account must be taken of both crystal thickness, which determines the importance of reabsorption of the fluorescence, and the limit of the solid solution, above which the characteristics are altered in a predictable manner by the formation of minute tetracene crystals in the structure.

V. ACKNOWLEDGMENT

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MIGRATION OF EXCITATION ENERGY IN ORGANIC CRYSTALS

II. SOLID SOLUTION OF ANTHRACENE AND TETRACENE IN NAPHTHALENE

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Summary

The migration of excitation energy from anthracene to tetracene has been studied in a solid solution of the two molecules in naphthalene crystal. Perturbation theory has been used to formulate the probability of transfer of energy from anthracene to tetracene when both are in naphthalene solid solution, and the excellent agreement with the experimental result (probability of fluorescence equals probability of transfer at an intermolecular distance of 44 Å) supports the conclusion that the mechanism operating is dominantly a non-radiative one, adequately described by the dipole-dipole approximation for the interaction between the molecules.

I. INTRODUCTION

In Part I of this series (Ferguson 1956), energy migration in crystals of anthracene containing minute amounts of tetracene was investigated. The efficiency of this process suggests that energy migration from anthracene to tetracene is feasible even if the molecules are farther apart than nearest neighbours in a crystal lattice. However, experiments designed to test this hypothesis in liquid solution (similar to those used so effectively by Förster (1949a, 1949b) for dyes) are limited by two factors: (i) low solubility, and (ii) the occurrence of fluorescence quenching. For these reasons, experiments were designed in which the anthracene and tetracene were dissolved in a solid solution of another hydrocarbon (naphthalene) and the present paper reports the results obtained, together with theoretical formulation and interpretation.

II. EXPERIMENTAL

The experimental method has already been related in Part I of this series. Consistent measurements were obtained from crystals grown from small amounts of each sample melted between silica disks on a hot-plate and then cooled to obtain thin sheets of the mixed crystals. Mixtures were prepared by dilution from an accurately prepared matrix containing 10^{-3} mole of both anthracene and tetracene per mole of naphthalene.

III. RESULTS

Figures 1 and 2 show the spectra excited by 3650 Å radiation in solid solutions having the following mole ratios equal in each component: 2×10^{-5} and 10^{-4} , and 3×10^{-4} , 5×10^{-4} , and 10^{-3} respectively. The dotted portions of

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the curves represent the most probable form of the emission in the region outside the limit of measurement. The peak positions are given in Table 1.

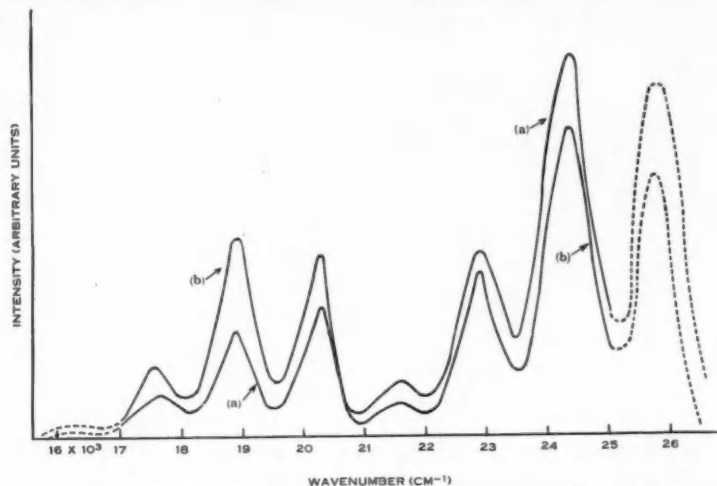


Fig. 1.—Fluorescence spectra excited from thin crystals of naphthalene containing equal amounts of anthracene and tetracene in mole ratios: (a) 2×10^{-5} and (b) 10^{-4} .

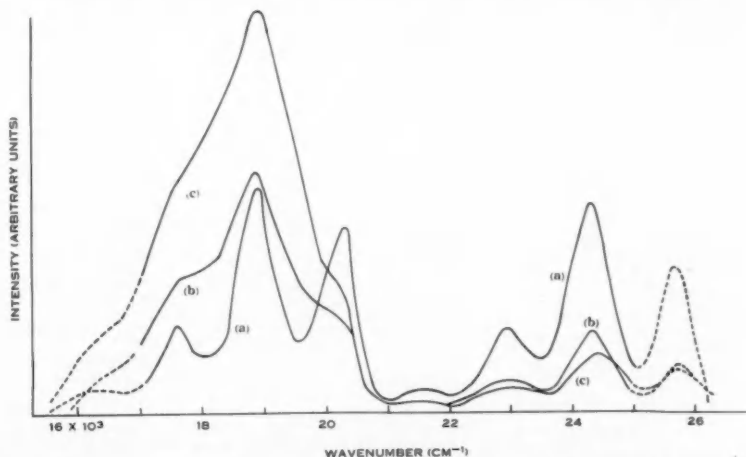


Fig. 2.—Fluorescence spectra excited from thin crystals of naphthalene containing equal amounts of anthracene and tetracene in mole ratios: (a) 3×10^{-4} , (b) 5×10^{-4} , and (c) 10^{-3} .

The diagrams show spectral intensity as a function of wavenumber and so the area under each curve is proportional to the total energy emitted. The fraction of the total energy emitted by the tetracene in each solution was

calculated by graphical integration and this fraction (expressed as the migration efficiency) is plotted *against* concentration (on a logarithmic scale) in Figure 3.

Figure 4 is analogous to Figure 4 of Part I (see p. 165) and shows the spectrum at room and low temperature emitted from a microcrystalline sample

TABLE I
PEAK POSITIONS OF THE FLUORESCENCE SPECTRUM
OF ANTHRACENE AND TETRACENE IN NAPHTHALENE
SOLID SOLUTION

Compound	Peak Position* (cm^{-1})
Anthracene	24,400
	22,900
	21,650
Tetracene	20,350
	18,950
	17,600

* All ± 50 .

having a mole ratio 3×10^{-4} of each component. The conclusions to be drawn are analogous, that is, decrease of temperature reduces the overlap between absorption and fluorescence spectra with subsequent rearranging of the intensity distribution.

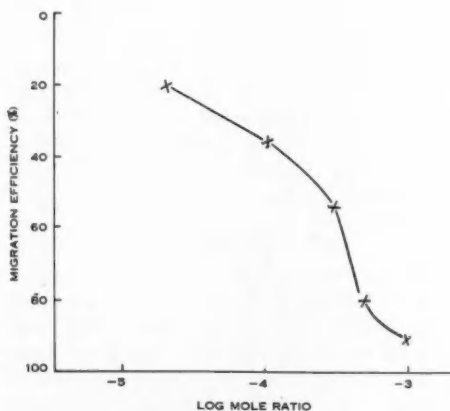


Fig. 3.—Migration efficiency as a function of the concentration.

Crystals of the highest concentration used were examined for homogeneity by measurement of their absorption spectra with a Beckman spectrophotometer from which the formation of crystalline tetracene, had it occurred, would have been easily detected (see Part I). The spectra were important moreover for

the determination of the spectral overlap integral used in the theoretical calculation outlined in Section IV. From these spectra and the fluorescence spectra a composite diagram was constructed, shown in Figure 5.

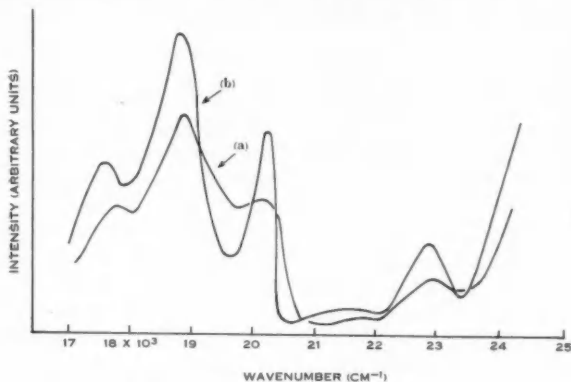


Fig. 4.—(a) Shows the spectrum at room temperature from a microcrystalline sample of mole ratio 3×10^{-4} , and (b) the same spectrum at -180°C without moving the sample.

In order to obtain information about the orientation of the impurity molecules in the naphthalene lattice, fluorescence measurements were made with polarized light and single crystals. These showed that a high degree of

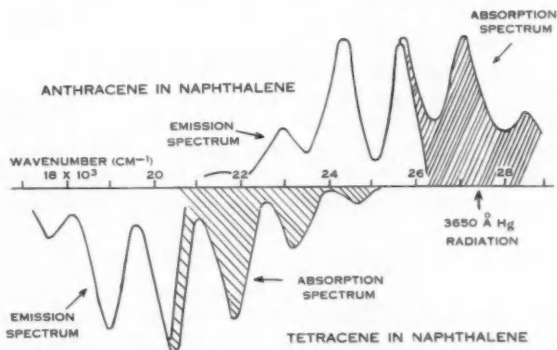


Fig. 5.—Absorption and fluorescence spectra of anthracene in naphthalene above the line, and of tetracene in naphthalene below the line.

uniformity exists in the positions taken up by the impurity molecules. The polarization ratios (b/a) are as high as 4.5:1 for both molecules, which is to be compared with an "oriented gas" value of 7:1 for a naphthalene molecule calculated from known crystal dimensions.

An attempt to study the efficiency of fluorescence as a function of the wavelength of the exciting radiation, as for tetracene in anthracene, was not feasible because of the low concentration of anthracene. (The maximum optical density for the thin crystals used was 0.17.)

IV. DISCUSSION

The measurements reported above show that energy originally absorbed by anthracene is transferred to tetracene with a very high efficiency in dilute solid solution. Geometrical arguments suffice to eliminate a radiative mechanism as detailed for the anthracene-tetracene crystals. The case against a photon mechanism is even more striking for these crystals in which the density of anthracene molecules in the light path is very much less than in the pure crystal. The anthracene fluorescence can no longer be considered as traversing the crystal because now only a fraction of the exciting light is absorbed by the thin crystals used. For example, a crystal with mole ratio 10^{-3} of each component had a maximum optical density of absorption for anthracene slightly less than 0.2, which means that only about 35 per cent. of the exciting radiation is absorbed by the anthracene, yet for this crystal 90 per cent. of the energy is emitted from the tetracene.

The failure of a radiative mechanism for energy migration leaves as the probable mechanism that of resonance transfer. The only published quantum mechanical treatment of resonance migration between complex molecules is that due to Förster (1947). This theory has been successful in its application to dye solutions, but Förster states that energy migration between molecules of the anthracene type will be restricted to intermolecular distances of the order 8–10 Å. This very low estimate is due to the restriction placed on the transfer process. Förster has not considered vibration and electronic interaction, so that the energy possessed by the excited molecule appears in the acceptor molecule only as electronic energy and not as a combination of electronic and vibrational energy. It seems more probable, however, that when the electronic excitation energy of the excited molecule is greater than that corresponding to the purely electronic excited state of the acceptor molecule, the difference in energy appears in the excitation of molecular vibrations, either in the donor or the acceptor molecule. The transfer process is completed then by the loss of this vibrational energy to the solvent medium.

The number and type of molecular vibrations excited will be determined by the rules which normally operate in absorption and emission of light by the respective molecules, that is, symmetry and the difference in size of the initial and final states. It is not necessary to include these factors explicitly because they determine the features of the absorption and emission bands of the molecules; they automatically enter into the expression for the transfer probability in its final form (see below). Dexter (1953) has recently given a thorough theoretical treatment of resonance migration in inorganic phosphors, and as this has wide generality the formulation will be used in the present work to facilitate cross reference.

According to perturbation theory in quantum mechanics (Dirac 1947; Schiff 1949) the transfer probability between two states of a system is

$$\frac{4\pi^2 t}{h} |\langle H' \rangle|^2 \rho_E,$$

where t is the time, ρ_E is the density of states, and $\langle H' \rangle$ is the matrix element of the perturbation between the initial and final states. In the present case, the initial state Φ_i has one molecule excited φ_s^1 , and the other is in its ground state φ_a^0 ; and the final state Φ_f is that in which the first molecule is in its ground state φ_s^0 , while the second is excited φ_a^1 . Then the probability per unit time that the energy is transferred from molecule s to molecule a is of the form

$$P_{if} = \frac{4\pi^2}{h} \rho_E \left| \int \Phi_i H' \Phi_f d\tau \right|^2.$$

The development of this expression to a form involving experimental parameters follows closely that given by Dexter (1953), except that the averaging over all orientations of the two molecules is omitted. The final expression for the probability of transfer of energy per unit time from molecule s to molecule a under the influence of the dipole-dipole interaction (dd) becomes

$$P_{sa}(dd) = \frac{9h^4 c^4 Q_a \Theta}{128\pi^5 R^6 n^4 \tau_s} \left(\frac{\xi}{x^3 \xi_c} \right)^4 \int \frac{f_s(E) F_a(E)}{E^4} dE, \dots\dots (1)$$

Θ is an orientation factor having the form:

$$(2 \cos \theta_{s1} \cos \theta_{a1} - \cos \theta_{s2} \cos \theta_{a2} - \cos \theta_{s3} \cos \theta_{a3})^2,$$

θ_{s1} , θ_{s2} , and θ_{s3} being the angles made by the transition moment of the sensitizer molecule with a set of rectangular axes erected at its centre; θ_{s1} refers to an axis along the line of the centres of the acceptor and sensitizer molecules. The other symbols in equation (1) denote the quantities defined by Dexter (1953).

The transfer probability is thus given by the strengths of the individual transitions in terms of the decay time and absorption band area Q and by the energy overlap of the absorption and emission bands of a and s respectively (the last term in (1)).

This formulation is perfectly general and can be applied to the system studied here. First, however, the expression must be reduced to a form more suitable to the experimental data. Figure 5 forms the basis for the calculation of the spectral overlap integral and as it was obtained from measurements in naphthalene as solvent the term n^4 , a corrective measure to account for the effect of the solvent, can be taken equal to unity. Further, the expression is more convenient in a form with wavenumber as the energy variable and extinction coefficient in place of absorption coefficient. Making the following substitutions:

$$Q = \int \sigma(E) dE, \sigma(E) = \frac{\epsilon(E) \ln 10}{6.02 \times 10^{20}}, E = hc\bar{\nu}, R = r \times 10^{-8}, \text{ and } \left(\frac{\xi}{x^3 \xi_c} \right)^4 = 1,$$

the transfer probability expression becomes

$$P_{sa}(dd) = \frac{8 \cdot 80 \times 10^{23} \times \Theta \times \int \epsilon_a(\bar{\nu}) d\bar{\nu}}{r^6 \times \tau_s} \int \frac{f_s(\bar{\nu}) F_d(\bar{\nu})}{\bar{\nu}^4} d\bar{\nu}. \quad \dots (2)$$

The spectral overlap integral was calculated by graphical integration and found to be $2 \cdot 01 \times 10^{-22} \text{ cm}^5$ and the well-known relationship

$$f = 4 \cdot 31 \times 10^{-9} \int \epsilon(\bar{\nu}) d\bar{\nu}$$

was used to calculate $\int \epsilon_a(\bar{\nu}) d\bar{\nu}$, taking $f = 0 \cdot 15$ for tetracene.

Substitution of these values into the transfer probability expression (2) yields

$$P_{AT}(dd) = \frac{6 \cdot 2 \times 10^9 \times \Theta}{\tau_A \times r^6}. \quad \dots (3)$$

Before using this equation, however, it is necessary to know whether anthracene-anthracene transfers will seriously interfere with results calculated for anthracene-tetracene transfers, because in the crystals used the anthracene and tetracene were present in equal concentrations. For this the spectral overlap integral was found to be $2 \cdot 5 \times 10^{-22} \text{ cm}^5$, and taking $f = 0 \cdot 1$ these yield

$$P_{AA}(dd) = \frac{5 \cdot 1 \times 10^9 \times \Theta}{\tau_A \times r^6}. \quad \dots (4)$$

Evidently the efficiency of the two processes will be the same order and if the results above are interpretable by the mechanism formulated here, then reasonably good agreement should be found between theoretical and experimental values even with the neglect of anthracene-anthracene transfers.

Figure 3 shows that at a mole ratio of each component of about $2 \cdot 5 \times 10^{-4}$, half of the emitted energy comes from the tetracene. Now the volume occupied by each naphthalene molecule in the naphthalene lattice is $181 \cdot 5 \text{ \AA}^3$, so the average concentration of the impurity molecules is one molecule per $45 \cdot 4 \times 10^4 \text{ \AA}^3$ at a mole ratio of $2 \cdot 5 \times 10^{-4}$ for each component. Setting this volume equal to $4\pi r^3/3$, the average intermolecular distance between impurity molecules is found to be 44 \AA . It remains to decide on a value for Θ to solve for the transfer probability during the fluorescence lifetime. The naphthalene lattice contains two sets of molecules in which the molecules of one set have their short axis nearly at right angles to the short axis of the molecules in the other set. From this and the large number of orientations possible for molecules at a distance of 44 \AA from an excited molecule the average value of Θ is found to be $2/3$.

Substitution for Θ and r leads to

$$P_{AT}(dd)\tau_A = 0 \cdot 6.$$

This value is in excellent agreement with the experimental result and strongly supports the conclusion, that the mechanism operating is dominantly a non-radiative one and is adequately described by the dipole-dipole approximation for the interaction between the molecules.

The success of this calculation and also the successful interpretation of the crystal spectrum of anthracene by Craig and Hobbins (1955) shows the dipole-dipole approximation to be very satisfactory for the interaction between excited and unexcited molecules, at least for the cases of most interest in molecular spectroscopy.

V. ACKNOWLEDGMENT

The author expresses his gratitude to Professor D. P. Craig for his interest, help, and many discussions.

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HEATS OF MIXING

II. ACETONITRILE AND NITROMETHANE SYSTEMS

By I. BROWN* and W. FOCK*

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Summary

The heats of mixing at 45.00 °C have been measured at intervals over the whole composition range for the systems: acetonitrile+carbon tetrachloride, acetonitrile+benzene, acetonitrile+nitromethane, nitromethane+carbon tetrachloride, and nitromethane+benzene. These data, together with the excess free energy data of Brown and Smith (1954, 1955a, 1955b), have been used to calculate the excess entropy of mixing for these systems.

I. INTRODUCTION

The heats of mixing of a number of systems containing polar components are being measured to permit the excess entropy of mixing of such systems to be calculated with greater accuracy than can be obtained from free energy data alone. These measurements form part of a programme to provide experimental thermodynamic data for testing theories of polar non-electrolytic solutions.

II. APPARATUS AND METHODS

The apparatus used was that described by Brown and Fock (1955). The only change in method was that the measured heating of the cell was done at the same time as the mixing, following the practice of Adcock and McGlashan (1954). The heater was switched on slightly before mixing so that approximately half the heat was introduced before mixing occurred. A second heating period 20 min after mixing provided a calibration for inexact compensation of the heat of mixing. This procedure reduces the errors due to extrapolation of the thermistor resistance-time curve.

TABLE I
PHYSICAL PROPERTIES OF COMPONENT LIQUIDS

Liquid	$n_{\text{D}}^{25.00}$	$d_4^{25.00}$
Acetonitrile	1.34157	0.77662
Nitromethane	1.37966	1.13062
Carbon tetrachloride	1.45734	1.58444
Benzene	1.49795	0.87362

III. COMPONENTS

The components were purified by the methods described by Brown and Smith (loc. cit.). The density and refractive index values are shown in Table I.

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IV. RESULTS

The mole fraction x_1 of the first mentioned component and the heat of mixing in J/mol of mixture are given in Tables 2, 3, and 4. The experimental

TABLE 2

HEAT OF MIXING OF ACETONITRILE SYSTEMS AT 45.00 °C

Acetonitrile + Carbon Tetrachloride		Acetonitrile + Benzene	
x_1	H_z^M (J/mol)	x_1	H_z^M (J/mol)
0.179	737	0.150	249
0.369	930	0.311	398
0.581	867	0.507	501
0.585	834	0.584	496
0.593	868	0.592	489
0.682	755	0.666	475
0.683	750	0.669	467
0.872	416	0.867	287

TABLE 3

HEAT OF MIXING OF NITROMETHANE SYSTEMS AT 45.00 °C

Nitromethane + Carbon Tetrachloride		Nitromethane + Benzene	
x_1	H_z^M (J/mol)	x_1	H_z^M (J/mol)
0.181	1017	0.173	428
0.211	1095	0.354	711
0.371	1367	0.579	824
0.436	1407	0.585	818
0.583	1377	0.666	775
0.595	1376	0.668	788
0.597	1346	0.865	463
0.687	1204		
0.844	773		

errors were estimated to be about ± 1.5 per cent. at $x_1 = 0.5$ and 2 per cent. near the extremities of the concentration range. For the system acetonitrile + nitromethane, however, the errors are approximately ± 2 J/mol.

TABLE 4

HEAT OF MIXING ACETONITRILE + NITROMETHANE AT 45.00 °C

x_1	H_x^M (J/mol)
0.246	+9.5
0.247	+7.8
0.441	0.0
0.445	0.0
0.553	+0.5
0.556	-2.2
0.750	+5.7
0.751	+5.6

Estimated error in $H_x^M = \pm 2$ (J/mol).

V. THERMODYNAMIC PROPERTIES

The excess free energy of mixing at 45.00 °C for these systems has been determined from liquid-vapour equilibrium data by Brown and Smith (loc. cit.). These data, together with the reported heat of mixing data, have been used to determine graphically at even mole fractions the excess free energy, heat, and

TABLE 5

THERMODYNAMIC PROPERTIES AT 45.00 °C (CAL/MOL)

x_1	Acetonitrile + Carbon Tetrachloride			Acetonitrile + Benzene		
	G_x^E	H_x^M	TS_x^E	G_x^E	H_x^M	TS_x^E
0.1	127	121	-6	63	43	-20
0.2	207	186	-21	108	73	-35
0.3	255	215	-40	138	93	-45
0.4	279	223	-56	155	107	-48
0.5	284	215	-69	161	115	-46
0.6	267	198	-69	155	117	-38
0.7	232	174	-58	138	110	-28
0.8	176	137	-39	107	90	-17
0.9	97	82	-15	60	55	-5

excess entropy of mixing of four of these systems at 45.00 °C. These data are given in cal/mol in Tables 5 and 6. The errors in TS_x^E shown in these tables have been estimated to be ± 8 cal/mol for the nitromethane + carbon tetrachloride system and ± 6 cal/mol for the other three.

$$1 \text{ cal} = 4.1840 \text{ J (abs.)}, \quad T \text{ } ^\circ\text{K} = t \text{ } ^\circ\text{C} + 273.16.$$

For the system acetonitrile+nitromethane at 60 °C the excess free energy of mixing is significantly zero over the whole concentration range. This indicates that the excess entropy of mixing (TS_x^E) for this system is not greater than +2.5 cal/mol or less than -1.0 cal/mol over the temperature range from 45 to 60 °C.

TABLE 6
THERMODYNAMIC PROPERTIES AT 45.00 °C (CAL/MOL)

x_1	Nitromethane + Carbon Tetrachloride			Nitromethane + Benzene		
	G_x^E	H_x^M	TS_x^E	G_x^E	H_x^M	TS_x^E
0.1	133	168	35	66	64	- 2
0.2	225	256	31	116	115	- 1
0.3	284	304	20	152	154	+ 2
0.4	313	332	19	174	181	+ 7
0.5	319	338	19	184	195	+11
0.6	302	321	19	179	195	+16
0.7	264	282	18	159	179	+20
0.8	204	219	15	124	145	+21
0.9	117	129	12	72	87	+15

VI. DISCUSSION

It is interesting to note that the excess entropy values for the acetonitrile systems are negative, and those for the nitromethane systems are positive, while the values for the acetonitrile+nitromethane system are substantially zero. No simple explanation of this is obvious at present. Measurements are being made on the corresponding systems with acetone as the polar component.

VII. ACKNOWLEDGMENTS

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NEW MOLECULAR COMPOUNDS OF THE LAYER LATTICE TYPE

I. NEW MOLECULAR COMPOUNDS OF GRAPHITE

By R. C. CROFT*

[Manuscript received November 15, 1955]

Summary

An extension of previous work (Croft 1952) on molecular compounds of graphite has led to the discovery of over 30 new molecular compounds of the layer lattice type.

In addition, the experimental data revealed some necessary conditions for compound formation. Thus, intercalation was found to be most probable with multivalent chlorides of the transition metals, but only when the latter are in their higher valence states. Chlorides of all Group IIIA elements can also form molecular compounds with graphite. Intercalation is related to the position of the cation of the test substance in the periodic table. Molecular shape, polarity, and the covalent nature of the test substance have little, if any, relation to its reactivity with graphite.

Graphite compounds formed from Group IIIA chlorides are distinguished from those containing transition metal chlorides by the possibility of hydrolysing intercalated cations of the former but not those of the latter. The metal cations of graphite- $ZrCl_4$ and graphite- YCl_3 are also capable of hydrolysis *in situ*.

The results of this investigation suggest the possibility of employing graphite compound formation to effect many chemical separations and purifications.

I. INTRODUCTION

Although for some time notable as the only known molecular compound of graphite, graphite-ferric chloride, discovered by Thiele (1932), no longer holds this unique position among the lamellar compounds of carbon. Recent research by the author (Croft 1952) revealed that anhydrous aluminium chloride forms a similar compound. Moreover, further experiments, based on the view that other substantially covalent chlorides might react with graphite, showed that molybdenum pentachloride, tungsten hexachloride, and uranium tetrachloride are also capable of intercalation. In addition, Croft and Thomas (1951) found that large quantities of chromyl chloride and chromyl fluoride can be rapidly intercalated in graphite.

Discovery of the new compounds mentioned above suggested that the formation of molecular compounds by graphite might be more general than previously supposed. It was decided therefore to test the reactivity of graphite to a wide range of substances. The latter were mostly chlorides because these appeared to be best suited to this type of examination. Results obtained from these investigations have been summarized already in a brief note (Croft 1953). However, the present paper gives the data fully, together with experimental details and conclusions on which are based the theories of intercalation developed in Part II of this series (Croft 1956).

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II. EXPERIMENTAL

The South Australian graphite used in the following experiments was obtained in a pure state from flotation concentrates, by treating the latter with concentrated HCl and HF alternately until the ash content was reduced to less than 0.02 per cent. ash. The purified material was then screened, the fraction between 65 and 100 mesh being retained. Dr. A. McL. Mathieson of this Division has kindly provided evidence to show that South Australian graphite treated in this manner consists of well-developed crystals, having the same structure as Ceylon and Madagascar graphite.

(a) Preparation of Test Substances

Test substances were of analytical reagent grade and were mostly obtained from approved suppliers. Some, however, were prepared by direct halogenation of pure metals or compounds of these.

Thus the anhydrous chlorides of Al, Fe, V, W, Cu, In, Re, Pd, and B were prepared by direct chlorination of the elements. UCl_4 was obtained by chlorinating a mixture of UO_2 with carbon. Oxychlorides of V, W, and U were prepared by chlorinating the metal oxides under appropriate conditions, while the chlorides of Zr and Hf were obtained by chlorinating the mixed carbides of these metals. The higher chlorides of Au and Pt were prepared by heating HAuCl_4 and H_2PtCl_6 respectively in a stream of chlorine gas.

Chlorides of the rare-earth elements were prepared from the oxides by repeated evaporation of the latter with concentrated A.R. hydrochloric acid. This method yields hydrated chlorides. However, it was decided to test reactivity of the latter with graphite before undertaking the tedious preparation of anhydrous chlorides. The purity of the oxides used in these preparations was as follows. Pr, Nd, Sm, Dy, Sc, and Yb oxides were all 97 ± 2 per cent. pure. The erbium oxide contained several per cent. of yttrium. The oxides of Y, La, and Ce were all 99 per cent. pure, while the Gd_2O_3 was pure as supplied by Messrs. Johnson and Matthey (London).

The chlorides of Co, Ni, and Cr were obtained in the anhydrous state by heating the hydrated chlorides in a stream of dry hydrogen chloride as described by Maier (1925). Where possible, volatile chlorides were purified either by sublimation or distillation in dry hydrogen chloride.

(b) Methods of Reacting Graphite with Test Substances

In most cases, intercalation tests were conducted by heating 0.5 to 1 g samples of graphite with three to four times their weight of the various chlorides in sealed Pyrex glass tubes for the periods and at the temperature shown in Table 1. These times and temperatures were selected as most suitable from the results of preliminary experiments. Chlorides reported as non-reactive were tested under a variety of times and temperatures above and below the experimental conditions given in the table. Considerable care was taken in preparing these tubes to maintain the anhydrous condition of the reactants. Thus, handling of reactants and filling of tubes was done in an atmosphere of dry nitrogen.

After heating, the contents of reaction tubes were washed with N/5 HCl to remove unreacted and absorbed chlorides, and after further washing with distilled water were (except in the case of the graphite- BCl_3 compound) dried at 110 °C. The graphite- BCl_3 compound was air dried on a sintered glass filter and was finally dried by storage over P_2O_5 .

In several cases it was necessary to react test substances with graphite by special methods. Thus the normally unstable chlorides CoCl_3 and PdCl_4 were produced in equilibrium with lower chlorides and caused to react with graphite by heating mixtures of the latter with CoCl_2 and PdCl_2 respectively in an atmosphere of chlorine. Another method, used in testing the reactivities of cupric, chromic, and bismuth chlorides towards graphite, consisted in chlorinating mixtures of graphite with the respective metals, the latter being in finely divided states. Since the reactions of these metals with chlorine are exothermic, it was not possible to exercise very much control over the temperatures at which the resulting chlorides reacted with the graphite. However, it was found that satisfactory results were obtained if the metal chlorinations were initiated at the lowest possible temperatures.

(c) Tests for the Intercalation of Test Substances in Graphite

Microscopic examination provided a helpful method for detecting the formation of graphite compounds, and little experience was necessary to permit easy recognition of the thickening of original flakes of graphite and teasing apart of the edges of the latter, both these observations being indicative of reaction.

Two more reliable tests were used, however, to confirm the formation of graphite compounds. Firstly, graphite, which was separated from contents of reaction tubes, was heated rapidly to approximately 700 °C to determine if it would exfoliate in the manner characteristic of known lamellar compounds of graphite. This test was performed on graphite which had been freed from unreacted test substance by washing successively with hot dilute HCl, water, and alcohol. The second test, which also served as a method of analysis, consisted in fuming a washed and dried sample of reacted graphite with conc. H_2SO_4 . The fumed sample was subsequently ashed at 850 °C for 12 hr and the residual oxide weighed and identified by chemical tests. In the case of compounds of graphite with rare-earth chlorides, this method was assumed to yield mixtures of basic and normal sulphate instead of oxides. Results relating to these compounds are therefore approximate and have been included only to indicate relative reactivity. In most instances chloride determinations were also performed in order to confirm the valence state of the cation of the intercalated chloride. In these analyses the graphite compound was decomposed by means of a Mahler bomb. Where it was possible to distil or sublime occluded material from a graphite compound and analyse it, a composition was also obtained for the graphite compound.

The results of the above tests and analyses are recorded in Table 1, which shows, in turn, the test substance heated with graphite, the temperature and period of heating, and finally, the results of intercalation tests. Since the object

TABLE I

RESULTS OF INTERCALATION TESTS WITH GRAPHITE

Substances Tested for Reaction with Graphite	Heated with Graphite		Exfoliation of Graphite on Subsequent Heating	Remarks
	Temperature (°C)	Time (hr)		
Group I				
LiCl ..	600	12	—	No reaction
NaCl ..	"	12	—	" "
KCl ..	"	12	—	" "
CuBr ₂ ..	340	2	+	Reacted graphite contained 4% CuBr ₂
CuCl ..	400	16	—	No reaction
CuCl ₂ ..	"	16	+	Graphite compound contained 4% CuCl ₂ (1 : 270)*
Cu + Cl ₂ + graphite }	Metal burned c. 600 °C		+	Reacted graphite contained 46% CuCl ₂ (1 : 13)
AgCl ..	400	16	—	No reaction
AuCl ₃ ..	300	3	+	Reacted graphite contained 45% AuCl ₃ (1 : 33) and exfoliated considerably on heating
Group II				
BeCl ₂ ..	350	4	—	None of these group II metal chlorides reacted with graphite
MgCl ₂ ..	450	12	—	
CaCl ₂ ..	"	12	—	
BaCl ₂ ..	"	12	—	
ZnCl ₂ ..	"	12	—	
CdCl ₂ ..	"	12	—	
CdI ₂ ..	"	12	—	
Hg ₂ Cl ₂ ..	"	12	—	
HgCl ₂ ..	"	12	—	
Group III				
BCl ₃ ..	12.5	2	+	Reacted graphite contained 11% BCl ₃ (1 : 79)
AlCl ₃ ..	250	4	+	Reacted graphite contained 25% AlCl ₃ (1 : 33)
AlBr ₃ ..	217	$\frac{1}{2}$	+	Reacted graphite contained 14% AlBr ₃ (1 : 137)
GaCl ₃ ..	180	1	+	Reacted graphite contained 11% GaCl ₃ (1 : 119)
InCl ₃ ..	360	12	+	Reacted graphite contained 51% InCl ₃ (1 : 18)
TiCl ₃ ..	105	17	+	Reacted graphite contained 70% TiCl ₃ (1 : 11)
ScCl ₃ ..	550	2	—	No reaction
YCl ₃ ..	"	40 min	+	Graphite compound contained 43% YCl ₃ (1 : 22)
LaCl ₃ ..	"	2	—	No reaction

* Atomic ratio cation to carbon.

TABLE I (Continued)

Substances Tested for Reaction with Graphite	Heated with Graphite		Exfoliation of Graphite on Subsequent Heating	Remarks
	Temperature (°C)	Time (hr)		
Lanthanons*				
CeCl ₃ ..	550	2	—	No reaction
PrCl ₃ ..	550	2	—	" "
NdCl ₃ ..	550	2	—	" "
SmCl ₃ ..	550	40 min	+	Reacted graphite contained approx. 38% SmCl ₃ (1 : 35) (see text)
EuCl ₃ ..	550	3	—	Reacted graphite contained approx. 3% EuCl ₃ (see text)
GdCl ₃ ..	550	2	+	Reacted graphite contained approx. 16% GdCl ₃ (1 : 115) (see text)
DyCl ₃ ..	560	2	+	Reacted graphite contained approx. 22% DyCl ₃ (1 : 79) (see text)
ErCl ₃ ..	560	2	(Slight)	No reaction
YbCl ₃ ..	560	2	—	Approx. 9% YbCl ₃ found in reacted graphite (see text)
Group IV				
CCl ₄ ..	90	24	—	No reaction
SiCl ₄ ..	20	48	—	" "
GeCl ₄ ..	85	3	—	" "
TiCl ₄ ..	110	1	—	" "
		month		
ZrCl ₄ ..	340	16	+	Reacted graphite contained 43.6% ZrCl ₄ (1 : 25)
SnCl ₂ ..	250	16	—	No reaction
SnCl ₄ ..	110	48	—	" "
HfCl ₄ † ..	340	17	+	Approx. 2% HfCl ₄ found in reacted graphite
PbCl ₂ ..	400	16	—	No reaction
PbCl ₄ ..	18	1	—	" "
ThCl ₄ ..	400	16	—	" "
ThI ₄ ..	300	4	—	" "
Group V				
PCl ₃ ..	64	12	—	No reaction
PCl ₅ ..	64	4	—	" "
	105	24		
PBr ₃ ..	100	1	Slight	Slight reaction due to Br ₂ liberated by thermal dissociation of PBr ₃
	180	1		
AsCl ₃ ..	140	16	—	No reaction
AsI ₃ ..	180	4	—	" "
SbCl ₃ ..	250	24	—	" "
SbCl ₅ ..	240	$\frac{1}{2}$	+	This salt was rapidly intercalated. The graphite compound contained 35% SbCl ₅ (1 : 46)
BiCl ₃ ..	350	16	—	No reaction

* All lanthanon chlorides were in hydrated condition.

† In presence of 50 times as much ZrCl₄.

TABLE I (Continued)

Substances Tested for Reaction with Graphite	Heated with Graphite		Exfoliation of Graphite on Subsequent Heating	Remarks
	Temperature (°C)	Time (hr)		
Group V (Continued)				
As + Cl ₂ + graphite	Metals burned reaction initiated c. 200		—	No reaction
Bi + Cl ₂ + graphite			Slight	Reacted graphite contained 37% Bi (1 : 18)
VCl ₄ ..	100	4	—	Trace V ₂ O ₅ obtained after fuming reacted graphite with H ₂ SO ₄ and ashing
VOCl ..	300	16	—	No reaction
VOCl ₂ ..	"	16	—	" "
VCl ₃ ..	{ 90 180	12	—	Partial oxidation of chloride led to result similar to that for VCl ₄
TaCl ₅ ..		4	+	Reacted graphite contained 44% TaCl ₅ (1 : 38)
Group VI				
SO ₂ Cl ₂ ..	64	4	—	No reaction
SOCl ₂ ..	64	4	—	" "
SeOCl ₂ ..	105	17	—	" "
TeCl ₄ ..	350	3	—	" "
CrCl ₃ ..	300	2	Slight	Graphite compound contained 4% CrCl ₃
Cr + Cl ₂ + graphite	{ Metal burned c. 600		Very slight	The graphite compound contained a remarkably high proportion of intercalated chloride, viz. 76% CrCl ₃ (1 : 4)
CrO ₂ Cl ₂ ..			4	+
CrO ₂ F ₂ ..	18	Almost spontaneous	+	Reaction of graphite with this salt was extremely fast. The reacted graphite which contained 40% CrO ₂ F ₂ (1 : 15), showed a greater degree of exfoliation on heating than was observed with any of the other molecular compounds
MoCl ₅ ..	300	16	+	The graphite compound contained 25% MoCl ₅ (1 : 68), which could be recovered unchanged by heating the compound above its formation temperature
WCl ₆ ..	320	7	+	Reacted graphite contained 26% WCl ₆ (1 : 94)
UCl ₄ ..	350	16	+	Reacted graphite contained 56% UCl ₄ (1 : 25)
UO ₂ Cl ₂ ..	300	16	+	Reaction confirmed by fuming reacted graphite with H ₂ SO ₄ then ashing; U ₂ O ₈ remained
Group VII				
MnCl ₂ ..	400	16	—	No reaction.
MnCl ₄ (?)	18	24	Very slight	Trace of MnO ₂ remained after H ₂ SO ₄ fuming and ashing of reacted graphite
ReCl ₄ ..	360	12	+	Reacted graphite contained 24% ReCl ₄ (1 : 87)

TABLE I (Continued)

Substances Tested for Reaction with Graphite	Heated with Graphite		Exfoliation of Graphite on Subsequent Heating	Remarks
	Temperature (°C)	Time (hr)		
Group VII (Continued)				
ICl ..	20	$\frac{1}{2}$	+	Reaction confirmed by recovery of iodine from reacted graphite
ICl ₃ ..	{ 20 90	3	+	Approx. 30% ICl ₃ (1 : 45) found in reacted graphite
		$\frac{3}{4}$	+	
Group VIII				
FeCl ₂ ..	{ 360 455	17	Slight	Slight reaction probably due to oxidation of FeCl ₂ . Variable amounts (2-4%) of FeCl ₃ found in reacted graphite
(FeCl ₃) ..		(12)	(Large)	
CoCl ₂ ..	340	12	—	No reaction
CoCl ₂ + Cl ₂	340	12	Slight	Graphite compound contained 55% CoCl ₂ (1 : 11)
NiCl ₂ ..	300	14	—	No reaction
RuCl ₃ ..	500	1	—	Reacted graphite contained 3% RuCl ₃
RhCl ₃ ..	500	4	—	Reacted graphite contained 14% RhCl ₃ (1 : 119)
PdCl ₂ ..	340	12	—	No reaction
PdCl ₂ + Cl ₂	340	3	+	54% PdCl ₄ (1 : 18) found in reacted graphite
OsCl ₄ ..	350	2	—	No reaction
IrCl ₄ ..	200	4	+	Graphite compound contained 20% IrCl ₄ (1 : 111)
PtCl ₂ ..	480	3	—	No reaction
PtCl ₄ ..	217	4	+	Reacted graphite contained 37% PtCl ₄ (1 : 48)

of the tests was to obtain unequivocal evidence of intercalation, but not optimum conditions for the latter, the compositions shown for various graphite compounds are not necessarily those corresponding with maximum intercalation.

III. DISCUSSION

The data collected in Table 1 lead to the following observations on the suitability of different classes of chlorides for occlusion in graphite.

- (i) With few exceptions, only the chlorides of transition metals and elements of Group III (B, Al, etc.) form molecular compounds with graphite.
- (ii) The valence state of the cation of a transition metal chloride determines whether or not reaction with graphite shall occur. Thus PtCl₄, PdCl₄, SbCl₅, and CuCl₂ are readily occluded but PtCl₂, PdCl₂, SbCl₃, and CuCl do not react even with wide variation of experimental conditions.
- (iii) As a result of several subsequent experiments it was found that some chlorides are capable of hydrolysis while intercalated in graphite. The chlorides of Al, Ga, In, Tl, Y, and Zr fall into this class.

The most evident conclusion to be drawn from the above observations is that high volatility, that is, mobility of a metal chloride, is not a prime condition for its intercalation in graphite. Failure to occlude the liquids TiCl_4 and SnCl_4 , and the successful intercalation of CrCl_3 and CuCl_2 , the latter pair being relatively not volatile at 600 °C, confirm this. The experimental work did show, however, that the rates of intercalation of test substances in graphite were related to their volatility. Hence, it was necessary to conduct some reactions at higher temperatures in order to obtain satisfactory rates of intercalation. It is interesting to note in this connection, that the method of preparing molecular compounds of CrCl_3 and CuCl_2 , by chlorinating the respective metals in the presence of graphite, resulted in very rapid intercalation rates compared with those obtained when graphite was simply heated with the anhydrous chlorides. It would seem that the exothermic reaction between chlorine and these metals may have maintained higher local temperatures and therefore greater chloride volatility. Alternately, it is possible that chloride molecules produced during chlorination of chromium and copper react with graphite before they have time to aggregate in a less reactive crystalline state. Again, the presence of chlorine may accelerate these reactions by causing shift of equilibria, for example, $\text{CrCl}_3 \rightleftharpoons \text{CrCl}_2 + \frac{1}{2}\text{Cl}_2$, in favour of the higher chloride. It is of interest to recall here the experimental observation that molecular compounds of graphite with CuCl_2 and CrCl_3 do not exfoliate on heating. This confirms the view expressed by Thiele (1932), that the spectacular vermiform expansion of graphite- FeCl_3 is due to the escape of intercalated FeCl_3 , vapour being hindered by a barrier formed by the strong bonding between peripheral atoms of adjacent carbon layer planes. Evidently, since CuCl_2 and CrCl_3 are both comparatively involatile substances, they do not exert sufficient vapour pressure in the interplanar spaces to cause these to be distended into the lenticular shapes found in exfoliated residues of the graphite- FeCl_3 compound.

The observation that the multivalent metal chlorides, that were successfully intercalated, all contained cations, which exhibited valencies greater than their usual least values, suggests that the reaction of these chlorides with graphite is due to the electronic configurations of their cations. This suggestion is consistent with the high specificity shown by graphite in its reactions.

Successful intercalation of AlCl_3 (typical of group IIIA chlorides) cannot be attributed to multivalence of the cation. However, since intercalated AlCl_3 may be hydrolysed *in situ*, it seems likely that the bonding between occluded AlCl_3 and graphite layer planes is different from that operating in the case of graphite- FeCl_3 which is unaffected by water. It is suggested, therefore, that compounds between graphite and AlCl_3 , GaCl_3 , InCl_3 , TiCl_3 , ZrCl_4 , and YCl_3 , all of which can be hydrolysed in the occluded state, constitute a distinct subgroup in the list of molecular compounds shown in Table 1.

Results of this investigation provide the necessary data for a theoretical examination of fundamental aspects of graphite compound formation given in Part II of this series (Croft 1956). In addition, however, they are of interest from an applied viewpoint. Thus, since graphite at most occludes insignificant quantities of chlorides which do not satisfy the criteria of intercalation mentioned

earlier, it is probable that graphite might be successfully used to purify those chlorides which can be readily intercalated in it. Consideration of Table 2, which summarizes intercalation test data in a more convenient form, indicates that the highly specific reaction between graphite and certain chlorides might be used in effecting separations of a wide variety of mixtures of anhydrous metal chlorides. Both these applications of the specific reactions of graphite in molecular compound formation are under investigation. It has been established already, however, that chlorides which are readily occluded do not, when mixed with an unreactive chloride, cause the latter to be simultaneously intercalated by an entraining mechanism which might perhaps be expected in cases where the chlorides are known to form double salts. These results, however, will be presented in detail later.

TABLE 2
SUMMARY OF INTERCALATION TEST RESULTS

Substances Intercalated in Graphite			Substances not Intercalated in Graphite			
CuCl ₂	SbCl ₃	RhCl ₃	CuCl	SiCl ₄	AsCl ₃	PdCl ₂
CuBr ₂	TaCl ₅	PdCl ₂ *	BeCl ₂	GeCl ₄	SbCl ₃	PtCl ₂
AuCl ₃	FeCl ₃ †	PtCl ₄	MgCl ₂	TiCl ₄	BiCl ₃	LaCl ₃
BCl ₃	CrCl ₃	ICl†	CaCl ₂	SnCl ₂	VCl ₄	CeCl ₃
AlCl ₃ †	CrO ₂ Cl ₂ †	ICl ₃	BaCl ₂	SnCl ₄	SO ₂ Cl ₂	PrCl ₃
AlBr ₃	CrO ₂ F ₂ †	YCl ₃	ZnCl ₂	PbCl ₂	SOCl ₂	NdCl ₃
GaCl ₃	MoCl ₅	SmCl ₃	CdCl ₂	PbCl ₄	SeOCl ₂	ErCl ₃
InCl ₃	WCl ₆	GdCl ₃	CdI ₂	ThCl ₄	TeCl ₄	ScCl ₃
TiCl ₃	UCl ₄	YbCl ₃	Hg ₂ Cl ₂	ThI ₄	MnCl ₂	
ZrCl ₄	UO ₂ Cl ₂	DyCl ₃	HgCl ₂	PCl ₃	CoCl ₂	
HfCl ₄	ReCl ₄	EuCl ₃	CCl ₄	PCl ₅	NiCl ₂	
	CoCl ₃ *					
	RuCl ₃					

* Normally unstable, but stable when intercalated in graphite.

† Previously known to react.

It should be noted that no attempts have been made in this work to find either optimum conditions for reaction or those conditions which favour maximum intercalation. All efforts have been directed to establishing beyond doubt whether graphite reacts with various test substances and negative results have been reexamined under the same variety of conditions as those employed to fully confirm positive results. Furthermore, the properties of new lamellar compounds have not yet been examined in detail. In this connection, however, it has already been confirmed that most of them possess high thermal stability and, except for compounds of the graphite-AlCl₃ type, are unaffected by a variety of solvents. It would appear, therefore, that the high thermal and chemical stability of graphite-FeCl₃ is generally characteristic of molecular compounds of graphite. This conclusion enhances the possibility, noted above, of employing the highly specific intercalation reactions of graphite for separation and purification of metals in the form of their anhydrous chlorides.

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NEW MOLECULAR COMPOUNDS OF THE LAYER LATTICE TYPE

II. THEORY OF FORMATION OF GRAPHITE COMPOUNDS

By R. C. CROFT*

[Manuscript received November 15, 1955]

Summary

Experimental results given in Part I of this series (Croft 1956a) have been examined theoretically with particular attention given to finding reasons for the specificity shown by graphite towards various chlorides. This specificity cannot be accounted for in terms of "molecular sieving" or polar interaction. It is suggested that intercalation involves transfer of electrons from the conducting band of graphite to cations of reactive chlorides.

Intercalation of transition metal chlorides can be correlated with possession of unsaturated penultimate electron shells by the cations concerned. However, correlation is only complete when the cations exhibit maximum electron affinities, as in their higher valence states.

Reaction of Group IIIA chlorides appears due to accommodation of electron pairs from the π band of graphite in $n(p)$ orbitals (or their hybrids) of the cations. The distinctive hydrolysis of these chlorides *in situ* indicates that graphite is a weaker donor than water.

Similar consideration of unreactive chlorides indicates that they are not intercalated because their cations are incapable of electronic interaction with graphite.

Several important conclusions, supported experimentally in Parts III and IV of this series (Croft 1956b, 1956c), have been drawn from these theoretical considerations. Firstly, since intercalation depends on electronic configurations of cations, any compound containing a suitable cation should be capable of intercalation in graphite irrespective of the anion associated with it. Secondly, provided they satisfy two conditions, other substances should be capable of intercalating foreign compounds in a similar manner to graphite. The necessary conditions are that a host substance is able to interact electronically with an intercalated substance, and that it must afford physical accommodation for the latter.

The potential value of graphite reactions, in elucidating fundamental problems, is also discussed.

I. DISCUSSION

The following theoretical treatment is designed to reveal fundamental aspects of the formation of molecular compounds of graphite.

There are three possible explanations of the remarkable specificity shown by graphite in its reactions with anhydrous chlorides. They are: (i) "molecular sieve" action (cf. Barrer 1945); (ii) dipole interaction, and (iii) charge transfer. Brief consideration of sizes, shapes, and polarities of molecules shown in Table 1 (Part I of this series, Croft 1956a) indicates that theories based on (i) and (ii) are untenable. Evidence in favour of (iii) is discussed.

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Intercalation of chlorides may be correlated with the positions of their cations in the periodic table and is therefore probably related to the outer electronic configurations of the cations concerned. Cations of successfully intercalated chlorides (excepting those of Group IIIA elements) all have incomplete penultimate electron shells in which electrons from the upper conducting band of graphite might be accommodated. This interpretation would require that these molecular compounds of graphite owe their existence to the transfer of π -electrons of graphite to incompletely filled electron shells of intercalated metal cations. The physical requirements of intercalation would readily be met by expansion of the graphite host structure normal to the carbon layers.

That high electron affinities of intercalated cations would assist electron transfer from graphite is confirmed by the experimental observation that only higher chlorides of transition metal chlorides are intercalated.

Two conditions therefore are necessary for intercalation. Firstly, electronic interaction between a cation and graphite must be possible, and secondly, the electron affinity of the cation must be sufficient to promote such interaction. These conditions, which are the basis of the specificity shown by graphite towards chlorides, are the same as those proposed by Mulliken (1950, 1952a, 1952b).

The probability that cations in graphite behave as electron acceptors is supported by evidence of their charge transfer reactivity obtained by Rabinowitch and Stockmayer (1942) and Orgel (1954, quoting Dainton). Moreover, observations by Evans and Uri (1949), Weyl (1951), and Dainton (1952) support the view that the valence state of the cation, decisive in graphite compound formation, is an important factor in charge transfer occurring with cations of transition metals.

The concurrence of views noted above suggests that the spectrographic expression (Orgel 1954) for the energy required to effect charge transfer,

$$W = E_A - I_D + \Delta,$$

where E_A is the electron affinity of the acceptor, I_D the ionization potential of the donor, and Δ the difference in energy of the reacting system, including environment, before and after transfer, should be applicable to the intercalation phenomenon shown by graphite. Interpretation of the experimental results as evidence of this suggests that intercalation occurs by reason of the low ionization potential of π -electrons of graphite and maximum electron affinities of cations which the latter show in their higher valence states. It also seems in view of the high density of mobile electrons on the carbon layer planes, that substantial values of Δ would be likely for the molecular compounds of graphite.

Experimental data (Table 1, Part I of this series, Croft 1956a) illustrate the significance of the two conditions for intercalation noted above. For example, the metal ion of cupric chloride, which can be intercalated, possesses one singly occupied $3d$ orbital in which an electron transferred from graphite might be accommodated. No such accommodation is available however in the saturated $3d$ shell of the cuprous iron nor is it possible to intercalate cuprous chloride. Similarly mercuric chloride in which the cation preserves the $5d$ shell intact is

not intercalated. Successful intercalation of cupric chloride indicates that the electron affinity of the cupric ion is sufficient to induce transfer. However, the close electron affinities of the cupric and mercuric ions, as indicated by second ionization potentials, show that electron affinity of a cation is not solely responsible for intercalation.

Electron affinity does determine intercalation when the cation possesses unsaturated penultimate electron shells in both higher and lower valence states. This is illustrated by the chlorides of iron. Magnetic susceptibility measurements show that the ferrous ion contains at least as many unpaired $3d$ electrons as the ferric ion. However, since only ferric chloride can be intercalated in graphite, it is evident that possession of singly occupied penultimate orbitals, though they represent possible accommodation for transferable electrons, does not alone guarantee intercalation, but to do so must be supported by a cationic electron affinity exceeding some minimum value. The electron affinity of the ferrous ion apparently lies below this critical minimum value.

The electronic structure of ferrocene (biscyclopentadienyl iron, Wilkinson *et al.* 1952) deduced by Dunitz and Orgel (1953) and Moffitt (1954) provides a marked contrast to that of graphite- FeCl_3 . It seems desirable to describe it here briefly because of the superficial, but spurious resemblance between graphite compounds and the "sandwich"-like biscyclopentadienyl compounds which at present are the subject of considerable interest. In diamagnetic ferrocene, the $3d$ orbitals of the iron atom sandwiched between parallel cyclopentadienyl radicals transform to symmetrical orbitals which overlap the $2p\pi$ -orbitals of each radical, thus giving rise to π -type covalent bonding. Though additional dative bonding is feasible, it is considered not to occur. Marked differences between stabilities and magnetic susceptibilities of ferrocene and graphite- FeCl_3 confirm that their electronic structures are completely different.

Failure to intercalate CoCl_2 , MnCl_2 , and NiCl_2 , though their cations possess unsaturated penultimate shells, is explained as for ferrous chloride. Intercalation of normally unstable CoCl_3 is attributed to stabilization of the cobaltic ion by reduction of its high electron affinity effected by charge transfer from graphite. These observations further support the view that there is a minimum value for the electron affinity of a cation and that intercalation occurs only when this is exceeded.

Elucidation of the manner in which charge is transferred from graphite to $(n-1)$ d -orbitals of transition metal cations awaits full investigation. At present, however, transfer would appear to occur via associated anions. This suggestion is consistent with the lack of correlation between intercalation and spatial configurations of chloride molecules. Observations on paramagnetic resonance, particularly those of Hennig (1954; also Owen and Stephens 1953) and Zener's (1951) and Zener and Heikes' (1953) interpretation of charge transfer in the solid state provide a reasonable basis for these views. The probability, voiced by Weyl (1951) and Hennig (1954), that high polarizability facilitates charge transfer over considerable distances also supports the above interpretation.

Results of current investigations show that magnetic susceptibilities of cations of intercalated transition metal chlorides are, with a few notable excep-

tions, almost the same as in the pure chlorides. Apparently, intercalation causes little disturbance of the electronic states of either cations or graphite layer planes and charge transfer in these cases must therefore be regarded as partial.

Although the foregoing arguments offer a satisfactory explanation of the formation of lamellar graphite compounds from transition metal chlorides in higher valence states, they are inapplicable to the intercalation of the Group IIIA chlorides. Cations of these chlorides can only interact with graphite by means of vacant valence orbitals which may accept paired but not single electrons from $2p$ π -orbitals of graphite. Interaction in this manner requires graphite to behave as an "onium" type donor as described by Mulliken and for convenience is referred to herein as "coordination". Use of the term in this sense does not necessarily imply orbital overlap. True coordination by graphite in its eminently ionic compounds with Group IIIA chlorides might however be justified in terms of "higher covalent" bonding proposed by Burstall and Nyholm (1952) as an alternative to Pauling's ionic bonding.

The intercalation of aluminium trichloride is typical for the Group IIIA chlorides. Wells (1945) notes that the Al^{+++} ion is octahedrally coordinated in the crystalline state, but that in the vapour state dimeric molecules exist by virtue of sp^3 bonding by the cations. Since aluminium chloride reacts with graphite at temperatures above the triple point of the former, there is no apparent reason to suppose that the type of bonding employed by the Al^{+++} ions reverts from sp^3 to sp^3d^2 on intercalation. Interaction between graphite and an intercalated Al^{+++} ion therefore appears to involve the third p -orbital previously employed by the ion in the formation of coordinate bonds in the dimeric chloride molecule.

Similarly, the well-known tendency of the trivalent boron ion to enhance its electron screening, by accommodating electron pairs of donor ligands in a readily invoked fourth sp^3 orbital, accounts for the intercalation of BCl_3 .

The probability that coordination by graphite involves p orbitals (or hybrids of these) of the Group IIIA cations is of interest because of failure to intercalate the tetrachlorides of silicon, germanium, tin, and lead. Nyholm (1954, personal communication) has suggested that the chlorides of these elements do not react with graphite because their cations offer only $n(d)$ - and $(n+1)$ -type orbitals for reaction and, although Trost (1952) has shown that these orbitals are used in the formation of addition compounds with various organic molecules, they are ineffectual when graphite is the ligand. As noted by Blumenthal (1954) tetravalent zirconium and hafnium (also yttrium) differ from titanium in that they are avid electron acceptors, hence intercalation of $ZrCl_4$, $HfCl_4$, and YCl_3 is consistent with the high electron affinities of their respective cations. Differences in the reactivities of Groups IIIA and IVA chlorides towards graphite apparently arises from variation of electron binding strengths of available cation valence orbitals. Craig *et al.*'s (1954) observation that outer d orbitals of sulphur, phosphorus, and similar elements are too diffuse to form useful bonds and the fact that chlorides of these elements do not react with graphite supports this explanation of differing reactivity.

Hydrolysis of intercalated chlorides, a distinguishing feature of the compounds formed between graphite and Group IIIA chlorides (also ZrCl_4 , HfCl_4 , and YCl_3), is apparently due to the ability of water molecules to usurp the coordinating role of graphite.

Although hydrolysis of intercalated BCl_3 necessarily involves $2p$ orbitals of the B^{+++} ion, and a similar mechanism is preferred for intercalated AlCl_3 , it is necessary to consider the possibility that hydrolysis of the latter can be explained according to Taube's (1952) theory of labile "outer" complexes. This explanation follows if, contrary to earlier conclusions, the intercalated Al^{+++} ion is assumed to be octahedrally coordinated by $3s3p^33d^2$ bonds as in crystalline AlCl_3 . The negative behaviour of compounds of transition metal chlorides with graphite cannot be interpreted in this manner. Thus, the magnetic susceptibility of the ferric ion in intercalated ferric chloride measured by Rüdorff and Schulz (1940) (and confirmed by the author) shows that this ion contains five unpaired electrons. If then, the ferric ion is octahedrally coordinated, it must, according to Burstall and Nyholm (1952), use $4s4p^34d^2$ orbitals. The complex which these bonds would enable it to form with chloride anions and graphite should be as labile and as easily hydrolysed as that suggested above for the Al^{+++} ion. Since intercalated ferric chloride is not hydrolysed it is clear that hydrolysis with Group IIIA chlorides, but not with transition metal chlorides, is not a matter of energetics relating to "inner" and "outer" complexes. Rather, this distinctive behaviour indicates that different types of electronic interaction of cations with graphite occurs with each class of chloride.

Until present investigations of structures and magnetic and electrical properties of graphite compounds are complete, little can be known of the effect of intercalation on graphite itself. However, an evident consequence likely to result from loss of electrons from the carbon layer planes is that interplane binding forces would be weakened and the planes therefore would be separated more easily. This suggestion is consistent with the observation that intercalation is usually accompanied by a ready increase of the spacing of crystalline graphite, generally from 3.35 to about 9 Å. A reason for this expansion is suggested by Brennan's (1952) account of the nature of the interplane forces. Brennan's view is that the forces which hold carbon layer planes parallel at distances of 3.35 Å in graphite are due to "instantaneous dipoles" which result from correlation of motions of mobile electrons in adjacent layer planes. According to this view it would appear that loss of mobile electrons or, perhaps more important, restriction of their motion by distributed positive charges on surfaces of the planes, must weaken the interplane forces. There is also the possibility that the plane binding interaction between Brennan's dipoles may be lessened when substances capable of some degree of induced polarization are intercalated between the planes.

II. CONCLUSION

Preceding arguments indicate that formation of compounds of graphite with various chlorides is due to the need of positive cores for maximum negative screening. Transition metal cations increase screening in penultimate electron shells by charge transfer. Group IIIA cations on the other hand accommodate

paired electrons from graphite in vacant valence orbitals. This interpretation leads to several important conclusions discussed below.

It would appear that any substance may intercalate other substances in the manner shown by graphite provided it satisfies the following requirements. Firstly, electronic interaction should be possible between the host substance and the substance to be intercalated. Secondly, a host substance must afford physical accommodation, that is, there must be accessible space within its structure in which the molecules, ions, or atoms of other substances can be accommodated. The case of graphite indicates that the actual dimensions of such space in the pure host substance are unimportant if the latter is capable of expanding them on intercalation. It should be noted that there is no evident reason why host substances must possess layer lattice structures as does graphite: provided the space within them is accessible, host compounds possessing cellular or semicellular structures ought, if they satisfy the above requirements, to be capable of intercalation.

It will be shown in Part IV of this series (Croft 1956c) that it has been possible to obtain experimental verification of the above generalization. A hitherto unknown series of lamellar type molecular compounds of boron nitride are reported and discussed in Part IV, and evidence of similar compounds of aluminium diboride and chromium trichloride is also noted.

Since the theories proposed to account for intercalation of both ferric and aluminium type chlorides in graphite depend entirely on the electronic configurations of cations of intercalated substances, it is evident that, if these theories are valid, it should be possible to intercalate the same cations associated with anions other than the chloride ion. It will be shown in Part III (Croft 1956b), that the above generalization is true of some oxides, sulphides, and oxychlorides.

Apart from the many possibilities, evident from the data in Table 2 (Croft 1956a, Part I) of using graphite compound formation as a method of separating or purifying the anhydrous chlorides of various elements, intercalation by graphite offers assistance in the elucidation of more fundamental problems. For example, it seems probable, for the rare earths (Sm, Yb, Eu) showing multivalence in consequence of promotion of 4f electrons, that intercalation of the chlorides of these elements results from the transfer of electrons from graphite to depleted 4f orbitals. However, it was found that $GdCl_3$ and $DyCl_3$ can also be intercalated. It would appear, therefore, by the preceding argument, that both Gd and Dy are potentially multivalent and that this property becomes apparent under the favourable condition of being intercalated as chlorides in graphite. Similar examples may be found in the actinon series, although for obvious reasons it would be difficult to obtain corresponding data for many of the elements in this group. Nevertheless, in view of the absence of reaction between $ThCl_4$ and graphite, the successful intercalation of UCl_4 would appear to support the recent chemical evidence of Glauekauf and McKay (1950) and the magnetic measurements of Dawson and Lister (1952), which indicate that the 5f orbitals of uranium may be used in formation of covalent bonds, and

hence are similar to penultimate electron shells of other transition elements as regards interaction with graphite.

It appears from results of current magnetochemical investigations that many of the intercalated transition metal cations are in a magnetically dilute state. Study of graphite compounds therefore offers a means of measuring the susceptibilities of these ions without incurring the discrepancies resulting from their mutual interaction. The paramagnetic tripositive gold ion, $m\mu_{\text{eff}}$ 2.45 B.M., was discovered by this means. Corresponding values for palladium and platinum ions in the higher valence states were similarly found to be 3.25 and 2.52 B.M., respectively.

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NEW MOLECULAR COMPOUNDS OF THE LAYER LATTICE TYPE

III. THE INTERCALATION OF METAL SULPHIDES AND OXIDES IN GRAPHITE

By R. C. CROFT*

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Summary

It has been shown that a number of sulphides and oxides of multivalent metals can be intercalated in graphite. The results of this investigation support the conclusion, reached in Part II of this series (Croft 1956a), that the electronic configuration of the cation of a compound determines the possibility of its intercalation, and that the nature of the anion has little significance. As in the case of chlorides reported in Part I of this series (Croft 1956b), the cations of intercalated sulphides and oxides are in higher valence states.

I. INTRODUCTION

Theoretical considerations recorded in Part II of this series (Croft 1956a) indicated that intercalation of chlorides in graphite is entirely dependent on electronic configuration of the cation. It was also noted as a corollary to this, that those cations which are readily occluded as chlorides ought also to be intercalated when associated with other anions, provided, of course, the compound representing this association is both stable and reasonably volatile. These conclusions suggested that the intercalation phenomenon shown by graphite is more general than indicated by results given in Part I of this series (Croft 1956b), and were therefore considered worthy of further investigation.

The present paper describes attempts to intercalate several sulphides and oxides, the cations of which have already been shown to be intercalated in graphite, when associated with the chloride ion.

II. EXPERIMENTAL

The South Australian graphite used in the following experiments was part of the purified and sized sample described in Part I in connexion with intercalation tests involving chlorides.

(a) Test Substances

All test substances were obtained in the purest form available, either as analytical reagent grade stock chemicals, or by preparation from pure metals using reagents of high purity.

Materials obtained from stock included Sb_2O_4 , MoO_3 , MoS_2 , and Sb_2S_5 .

Sulphides of the metals Cr and W were prepared by direct union of the elements at approximately 700 °C. In both cases it was necessary to mix the

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product of the first heating with additional sulphur, resealed in a silica tube, and again heat at the reaction temperature.' Two repetitions of this procedure were necessary to ensure complete reaction.

Tl₂S was precipitated by H₂S from cold Tl₂SO₄ solution containing a trace of H₂SO₄, and PdS was obtained in a similar manner from an acidified solution of PdCl₂.

Heating V₂O₅ in a stream of H₂S at 850 °C was found to be the most satisfactory method for preparing V₂S₃.

Fresh CrO₃ was prepared in the usual manner by precipitation from a saturated solution of K₂Cr₂O₇ with concentrated H₂SO₄. The product was washed with concentrated HNO₃, then dried at 150 °C.

(b) *Reactions with Graphite*

The above substances were reacted with graphite by heating in sealed Pyrex glass tubes as described in Part I. The reaction times and temperatures were selected as the most suitable from results of preliminary tests, and it should be emphasized that they do not necessarily correspond with conditions for maximum intercalation.

Excess sulphur was added to mixtures of sulphides and graphite because initial crystallization experiments with the former indicated that their cations possess substantial mobility in the presence of sulphur at elevated temperatures.

After heating, the contents of the tubes were extracted with CS₂ to remove sulphur. Residues remaining from these extractions were ground lightly by hand and wet screened until all particles of free sulphide had been washed through the screen. This separation was possible since all test sulphides were in a finely divided form when added to the reaction tubes. Purification of the reacted graphite was effected by hand separation, under a binocular microscope, followed by digestion of the separated material with 6N nitric acid. Since partial decomposition results from digestion, the latter was necessarily limited in some cases.

Graphite reacted with Sb₂O₄ was purified by the same method as used for sulphide experiments. Excess MoO₃ associated with graphite in the tube in which these substances were heated together was successfully separated from the reacted graphite by controlled sublimation performed before the tube was opened. The last traces of free MoO₃ were then removed by washing with dilute NH₄OH. Unreacted CrO₃ was also separated from the graphite-CrO₃ compound by dilute acid and water washing.

Besides heating with test substances in sealed tubes, samples of graphite were also mixed with solid K₂Cr₂O₇ and Ba(MnO₄)₂, these mixtures being moistened with concentrated H₂SO₄, then allowed to stand approximately 1 hr at room temperature. Finally, the reacted graphites from these experiments were thoroughly washed with water, dilute HCl and water, then dried with alcohol and ether.

(c) *Examination of Products*

Graphite compounds obtained from the above tests were decomposed by oxidation in a Mahler bomb. Standard analytical methods for the determination

TABLE I
INTERCALATION OF SULPHIDES AND OXIDES IN GRAPHITE

Test Compound	Composition of Reaction Mixture	Heated		% Composition of Reacted Graphite after Washing			Empirical Formula of Intercalated Metal Sulphide	Remarks
		At (°C)	For (hr)	Metal	S	C		
S ..	Reactants mixed in ratio S : graphite 1 : 1	510	16	—	0.00	99.87	—	—
Sb ₂ S ₃ ..	BDH ex-stock mixed with equal weight of graphite	510	17	5.80	3.60	90.60*	Sb ₂ S _{4.8}	—
Tl ₂ S ..	Mixture of Tl ₂ S, S, and graphite in ratio 1 : 1 : 1.7 heated together	200	17	20.60	6.45	72.95*	TlS ₂	Subsequent heating of the washed graphite-TlS ₂ compound resulted in pronounced exfoliation
Cu+S ..	Cu powder, S, and graphite mixed in ratio 2 : 3 : 1	520	17	9.75	6.45	83.80*	CuS _{1.3}	Washed graphite-CuS compound swelled on subsequent heating
Fe+S ..	Fe powder, S, and graphite mixed in ratio 2 : 4 : 1	480	48	5.70	6.54	87.76*	FeS ₂	Washed graphite-FeS ₂ compound swelled rapidly on subsequent heating
Cr ₂ S ₃ ..	Cr ₂ S ₃ , S, and graphite mixed in ratio 1 : 2 : 1	560	120	1.93	2.08	95.99	Cr ₂ S _{2.3}	—
V ₂ S ₃ ..	Reactants mixed in equal portions	570	137	1.77	1.95	96.28*	V ₂ S _{3.5}	—
MoS ₂ ..	MoS ₂ , S, and graphite in ratio 5 : 3 : 3	570	48	0.32	0.23	99.45	—	—
WS ₂ ..	Reactants mixed in equal portions	570	137	10.02	4.09	85.89*	WS _{2.4}	A blue iridescence noticeable on surface of the washed compound
PdS ..	PdS, S, and graphite mixed in ratio 1 : 2 : 1	570	137	5.30	3.50	91.20*	PdS _{2.2}	—
Sb ₂ O ₄ ..	Four parts Sb ₂ O ₄ mixed with one of graphite	520	17	1.08	0.28*	98.64	Sb ₂ O ₄	Flake-like pseudomorphs of Sb ₂ O ₄ obtained on ashing graphite compound
CrO ₃ ..	Oxide and graphite mixed in ratio 2 : 1	198	48	28.60	26.4*	45.00	CrO ₃	No evidence of graphite having been oxidized to CO or CO ₂
MoO ₃ ..	Same as for CrO ₃	520	17	7.18	3.57*	89.25	MoO ₃	MoO ₃ can be recovered by sublimation, when the graphite compound is heated at about 700°C in air
K ₂ Cr ₂ O ₇ + conc. H ₂ SO ₄	Graphite mixed with equal weight of salt then moistened with acid	18	1	1.56	—	—	—	Pseudomorphs of metal oxide remained after ashing the treated graphite
Ba(MnO ₄) ₂ + conc. H ₂ SO ₄	As for K ₂ Cr ₂ O ₇	18	1	2.46	—	—	—	Same as for Cr, above

* Determined by difference.

of metals, sulphur, and carbon were then applied. In some cases carbon was determined by difference.

The results of these analyses are shown in Table 1, which also indicates reaction conditions, and observations on products. Preliminary X-ray examination of some of the products yielded very complex diffraction patterns, which require further study. However, patterns obtained for products of graphite-sulphide reactions do not correspond with those of lower sulphides. For products resulting from graphite-oxide reactions, graphite plane spacings as high as 11 to 12 Å were recorded.

III. DISCUSSION

The results of the experiments described above amply confirm the claim that the electronic configuration of cations of substances is of prime importance with respect to the intercalation of these substances in graphite. It is also evident from Table 1, that the cations of chlorides shown to be intercalated (Part I) can be made to react similarly with graphite when associated with sulphur and oxygen anions. A further important point arising from these data is that, as for chlorides, the cations of intercalated sulphides and oxides are in higher valence states.

No significance is attached to failure of analytical data to yield rational empirical formulae for the intercalated sulphides. The metal sulphides are notable for their non-stoichiometric compositions. It is possible that molecular sulphur was also intercalated, notwithstanding the negative result recorded for graphite and sulphur alone. Variations in these compositions are not, however, of sufficient magnitude to invalidate the preceding observation regarding valence states.

It would appear that the suggestion offered, in the case of some chlorides (PdCl_2 and CoCl_2), to account for the intercalation of higher chlorides, also applies to sulphides. Thus it seems probable that a lower sulphide yields equilibrium amounts of higher sulphides, when heated with sulphur, and that these higher sulphides are steadily removed by intercalation in the graphite also present.

The properties of the various lamellar compounds of graphite with sulphides and oxides, generally, resemble those observed for molecular compounds of chlorides with graphite. A number of the graphite-sulphide complexes swelled on strong heating, graphite- CrO_3 showing marked exfoliation. The blue iridescence of the graphite observed on the intercalation of many chlorides was observed with most of the sulphides and with CrO_3 . Similarly, the flake-like pseudomorphs of Cr_2O_3 , obtained when graphite- CrCl_3 is ignited after fuming with concentrated H_2SO_4 , were also obtained when graphite- Cr_2S_3 and graphite- CrO_3 were decomposed by the same method. Graphite- CuS and graphite- Sb_2O_4 also gave pseudomorphs of CuO and Sb_2O_4 respectively. In the case of MoO_3 which was the only sufficiently stable test substance, it was found possible to recover MoO_3 from graphite- MoO_3 by sublimation. Graphite- FeS_2 and graphite- CuS are both decomposed by prolonged treatment with hot dilute acids.

The experimental observation, that graphite and CrO_3 can be heated together at temperatures up to 200°C without apparent oxidation of the former, appeared to refute Hofmann's (1937) view that graphite is only oxidized by mixtures of concentrated H_2SO_4 with either $\text{K}_2\text{Cr}_2\text{O}_7$ or $\text{Ba}(\text{MnO}_4)_2$. The detection of measurable quantities of Cr and Mn, in samples of graphite treated with these mixtures, supports this conclusion, and suggests that CrO_3 and Mn_2O_7 , liberated by the action of concentrated H_2SO_4 on the respective salts, are simultaneously intercalated by the graphite. Inability to eliminate Cr and Mn by prolonged washing, which decomposes all known graphite salts, discounts the possibility that the above treatments yielded salts of graphite containing CrO_4^- and MnO_4^- anions.

IV. ACKNOWLEDGMENTS

The author expresses his thanks to Mr. L. J. Rogers for his assistance with analyses and the preparation of some of the sulphides used as test substances. He also wishes to thank Mr. A. J. Gaskin and Dr. G. F. Walker for undertaking the X-ray examination of products.

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NEW MOLECULAR COMPOUNDS OF THE LAYER LATTICE TYPE

IV. NEW MOLECULAR COMPOUNDS OF BORON NITRIDE

By R. C. CROFT*

[Manuscript received November 15, 1955]

Summary

Conclusions, arising from theoretical treatment of data obtained for graphite, indicated that the formation of intercalation compounds should also be possible with other crystalline materials possessing accessible intracrystalline space and the capacity for electronic interaction with intercalated substances.

Crystalline boron nitride, which is notable as a structural analogue of graphite, was selected as one of the materials with which to test this hypothesis.

Electronic interaction between boron nitride and intercalated substances appeared possible by means of either (i) electron transfer involving normally latent fourth sp^3 boron bonds, or (ii) coordination of intercalated cations by unshared pairs of nitrogen valence electrons.

The experimental results confirmed these conclusions.

Failure to intercalate boron trifluoride and boron trichloride in boron nitride suggests that the unshared pairs of nitrogen valence electrons are partially conjugated in the boron nitride planes.

Results of this investigation strongly favour the view that molecular intercalation shown by graphite is a general phenomenon, likely to occur with any other crystalline substance which satisfies the two necessary conditions noted earlier.

I. INTRODUCTION

In Part II of this series (Croft 1956a), it was suggested that the criteria of intercalation found to hold for graphite should also be applicable to other crystalline materials. In particular, substances possessing accessible intracrystalline space, and the capacity for electronic interaction with foreign molecules should also exhibit the intercalation phenomenon.

Investigation of this possibility was conducted on similar lines to those described for graphite in Part I (Croft 1956b). In this case, however, crystalline boron nitride was tested as the host substance.

II. THEORETICAL

Boron nitride is of particular interest in relation to the intercalation phenomenon because it is the classical structural analogue of graphite. The boron and nitrogen atoms comprising it are linked in hexagonal rings to form extensive two-dimensional planes, similar to those of graphite and possessing comparable stability. Also, as in graphite, these planes are stacked in parallel

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positions and so maintained by relatively weak interplane forces. Crystalline boron nitride therefore can offer spatial-accommodation, similar to graphite, to foreign molecules if these are otherwise eligible for intercalation.

Ability of boron nitride to interact electronically with intercalated substances (a necessary condition for the formation of graphite compounds) would be expected because of the well-known electron accepting property of the boron ion. According to Pauling (1948), the trivalent ion readily forms four sp^3 hybrid bonds if it is possible to stabilize one of these with donated electrons. In addition, the unshared pairs of valence electrons on the nitrogen atoms of the nitride might also be capable of coordinating intercalated substances possessing suitable vacant orbitals.

The possibility that boron favours some measure of tetrahedral bonding in boron nitride suggests a similarity between the bonding habits of boron and those of graphitic carbon. If this is correct B—N bonds might be expected to show some double bond character associated with the system B^- and N^+ . Studies on the band structure of BN by Taylor and Coulson (1952) support this view. The results of Becher and Gubeau (1952) provide more definite confirmation of this conjugation of unshared electron pairs of the nitrogen in the BN planes. This structure would involve partial occupation of the boron sp orbitals normal to the planes, this arrangement being analogous to that of graphite. Therefore, as in the case of graphite, these normally disposed boron $2p$ orbitals would be expected to play an important part in the electronic mechanisms of intercalation.

III. EXPERIMENTAL

(a) Preparation of Boron Nitride

This compound was prepared in a crystalline state from analytical reagent grade amorphous material by high temperature treatment according to the method described by Pease (1952). The crystalline material was obtained in both lamellar and "massive" forms, but each showed easy cleavage and the 120° surface lines on basal planes as frequently seen on macrocrystalline graphite. In agreement with the description given by Ephraim (1943), the crystalline boron nitride was black and lustrous and lamellae were easily bent as is true for graphite. On chemical analysis it was found to contain not more than 0.75 per cent. of impurities. The compositions of these were not determined.

(b) Test Compounds

The substances used in intercalation tests were all analytical reagent grade or, in the case of chlorides of copper, iron, and aluminium, were prepared by chlorination of pure metals.

Cylinder ammonia was used, while anhydrous hydrazine was obtained from hydrazine hydrate by fractionation with solid sodium hydroxide.

The method of reacting test substances with crystalline boron nitride consisted, as in graphite experiments, of sealing the reactants in evacuated Pyrex glass tubes and heating the latter for specified times at predetermined temperatures. The temperatures and periods of heating were selected according to the results of preliminary tests to determine suitable conditions.



Fig. 1.—BN-FeCl₃: (a) before, (b) after exfoliation ($\times 30$).



Fig. 2.—BN-AlCl₃: (a) before, (b) after exfoliation ($\times 30$).



Fig. 3.—BN-(NH₄)₂: (a) before, (b) after exfoliation ($\times 30$).



Fig. 4.—Graphite-FeCl₃: (a) before, (b) after exfoliation ($\times 30$).

(c) *Detection and Estimation of Reaction*

As for graphite, some cases of intercalation of test substances in boron nitride could be detected by loss of lustre and teasing of the edges of lamellae, both these effects being readily observed under a low power microscope. Rapid heating of reaction products to cause exfoliation was also used as a test for intercalation.

TABLE I

RESULTS OF INTERCALATION TESTS WITH BORON NITRIDE

Test Compound	Heated with Boron Nitride		% Test Substance found in Boron Nitride after Washing	Remarks
	Temperature (°C)	Time (hr)		
SbCl ₅ ..	118	12	Nil	Lustre of BN decreased after heating with test substance
SbCl ₃ ..	250	12	2	
AsCl ₃ ..	118	12	4	" " " "
CuCl ..	400	12	5	
CuCl ₂ ..	400	12	Nil	" " " "
Br ₂ ..	75-80	24	Nil	
ICl ..	75-80	24	Nil	Appearance of BN unchanged
FeCl ₃ ..	400	12	10.6	Lustre of BN decreased
				BN expanded and assumed a matt appearance during heating. After washing, it exfoliated on subsequent heating to approx. 600 °C (see Fig. 1)
AlCl ₃ ..	250	12	13.0	BN expanded during heating and acquired an iridescent appearance. Subsequent heating of the washed sample resulted in exfoliation (see Fig. 2)
NH ₃ (liquid)	-77.7	10 min	Nil	BN unchanged
	Room temp.	1 day	Nil	BN unchanged
NH ₂ .NH ₂	98	12	2	BN expanded and assumed dull matt appearance on heating. Considerable exfoliation occurred when the washed sample was heated (see Fig. 3)
BCl ₃ ..	57	21	Nil	Appearance of BN unchanged
BF ₃ ..	101	15 min	Nil	Appearance of BN unchanged

Quantitative estimation of the extent of intercalation was made by measuring the increase in weight of boron nitride samples after they had been reacted then washed with dilute HCl (except for the ammonia and hydrazine tests) and distilled water, and dried either in the oven at 110 °C or over P₂O₅. The results obtained by this method were confirmed by analysis in which standard methods were applied to aqueous solutions of melts obtained by fusing reacted and washed boron nitride with sodium peroxide in covered nickel crucibles.

The compound of boron nitride with hydrazine was analysed by destructive distillation, the distillate being trapped in a liquid air trap, dissolved in water, and then estimated volumetrically with $N/100$ HCl.

Conditions under which tests were performed and the results of examinations made on the reaction products obtained from these are shown in the following Table 1. Photographs of exfoliated boron nitride, resulting from rapid heating of several of its lamellar compounds, are shown in Figures 1, 2, and 3. Figure 4 showing a similar form of graphite obtained by heating graphite-ferrie chloride is included for comparison.

IV. DISCUSSION

It will be seen from the results given above that the molecular compounds of boron nitride are very like those of graphite. They show the same high stability to heat and solvents. Furthermore, on strong heating, they exfoliate in the manner characteristic of lamellar compounds of carbon and, as is true for the latter, they also yield the intercalated substance in its original form.

These observations confirm the predicted ability of boron nitride to intercalate other substances. That this process involves electron transfer, theoretically only probable with boron nitride planes as acceptors, is substantiated by the fact that the lower chlorides of multivalent cations are intercalated. In graphite, the carbon layer planes behave as electron donors and this substance therefore occludes only the higher chlorides of the same cation. Boron nitride is, therefore, as required by theory, complementary in behaviour to graphite in its reactions with multivalent metal cations (provided no coordination by layer plane nitrogen atoms exists, as described below).

The successful intercalation of aluminium chloride in boron nitride is significant because, since there is no possibility of electron transfer from the boron nitride planes to the aluminium cations interposed between them, it appears that the latter are attached to the layer planes by semipolar bonds resulting from coordination of the $3p$ orbitals of the aluminium by unshared pairs of nitrogen valence electrons. This explanation is analogous with and supports that which the author has already proposed for graphite (see Part II).

Since charge transfer is not feasible as in the case of graphite, intercalation of ferrie chloride is also considered to be due to similar coordination of the ferrie ions.

At first sight, it would be expected that boron trifluoride and boron trichloride, both known to form many molecular addition compounds by semipolar bonding, should be as capable of intercalation in boron nitride as is aluminium chloride. The successful occlusion of boron trichloride in graphite supports this view. Reasons for the different behaviour of the boron halides compared with that of $AlCl_3$ and $FeCl_3$ are not apparent.

Experimental data presented herein confirm the original contention (Part II), that the intercalation phenomenon exhibited by graphite is general in character and can be expected wherever the requirements of electronic reactivity and intracrystalline space are satisfied.

Results from current investigations also support this generalization. For example, AlB_2 and CrCl_3 , both possess layer lattice structures, have each shown evidence of ability to form lamellar compounds. The former reacts with ammonia while CrCl_3 forms compounds with MoCl_5 containing up to 40 per cent. of the latter.

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INTERACTION OF SODIUM DODECYL SULPHATE WITH A SOLUBLE KERATIN

By I. J. O'DONNELL* and E. F. WOODS*

[Manuscript received November 2, 1955]

Summary

Electrophoretic studies have shown that sodium dodecyl sulphate combines with α -keratose in solution in amount far in excess of that required for stoichiometric binding to the positive groups on the protein. However, an amount equivalent to the number of positive sites on the protein is more firmly bound than the remainder.

The variation of the relative viscosity and sedimentation coefficients with the amount of sodium dodecyl sulphate present on the protein has been attributed to changes in the configuration and state of aggregation of the protein molecules.

A molecular weight of approximately 48,000 has been determined for α -keratose in the presence of sodium dodecyl sulphate.

I. INTRODUCTION

When sodium dodecyl sulphate (NaDDS) was added to α -keratose, a protein fraction prepared from wool after oxidation with peracetic acid, the ultracentrifuge pattern underwent a marked change from two sedimenting peaks into single-boundaried form (O'Donnell and Woods 1955). This change was accompanied by a marked decrease in viscosity and was attributed to a disaggregation of the protein molecules.

α -Keratose contains a large number of $-\text{SO}_3\text{H}$ groups from the oxidation of cystine residues, and its interaction with sodium dodecyl sulphate, also containing a strong acid group, is of interest. The present paper gives the results of electrophoresis, viscosity, and sedimentation studies on the interaction of NaDDS with α -keratose.

II. EXPERIMENTAL

(a) Materials

The α -keratose was the same preparation (C36) as used in a previous study by the authors (O'Donnell and Woods 1955). Its refractive increment in 0.2 ionic strength phosphate buffer pH 6.7 was 0.00192.

Pure sodium dodecyl sulphate was prepared by the method of Dreger *et al.* (1944) from Eastman Kodak dodecyl alcohol and was completely dialysable through cellophane tubing (Harrap and O'Donnell 1954). Its refractive increment was 0.00113. A phosphate-NaCl buffer of ionic strength 0.2, pH 6.7 consisting of 0.0125M Na_2HPO_4 , 0.0125M NaH_2PO_4 , and 0.15M NaCl was used throughout most of this work. NaCl was added where higher ionic strengths

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were required. Potassium salts could not be included in buffer solutions with sodium dodecyl sulphate because of the insolubility of potassium dodecyl sulphate.

(b) Methods

(i) Electrophoresis was carried out in the Tiselius apparatus using the combined Schlieren optics and the multi-fringe Rayleigh interference patterns as described by Svensson (1951). The relative amounts of components were obtained by counting the number of fringes crossed between successive minima, the minima being determined from the gradient curve. All results are quoted in terms of numbers of fringes. The total number of fringes in each pattern can also be determined from the relation

$$J = a(\Delta n/\lambda),$$

where Δn is the refractive index increment of the solution, a the thickness of cell in direction of the optic axis, and λ the wavelength of light used (5460 Å). There was satisfactory agreement between the total number of fringes calculated from Δn which was measured independently, and that obtained from the electrophoretic patterns.

Mobilities were calculated from the slope of the distance-time graph for each peak.

The protein solution used was exhaustively dialysed against the 0.2 ionic strength buffer and weighed amounts of NaDDS added to the protein 24 hr before electrophoresis. Provided the amount of NaDDS did not exceed 0.25 g/g protein, electrophoresis could be done at 1 °C, but, at higher ratios of detergent, NaDDS precipitated, and above this amount electrophoresis was therefore performed at 18 °C. The field strengths used were 4 V/cm at 1 °C and 1 V/cm at 18 °C; conductivities of the solutions were measured at 0 and 18 °C respectively.

(ii) Refractive index increments were measured in a refractometer of the type described by Cecil and Ogston (1951), the concentration of protein being determined initially by the Kjeldahl procedure.

(iii) Viscosities were measured in an Ostwald capillary viscometer having a time of flow with water of 230 sec.

(iv) Sedimentation coefficients were measured with a Phywe air-driven ultracentrifuge at 830 rev/sec, the Schlieren optical system being used to obtain records.

III. RESULTS AND DISCUSSION

(a) Electrophoresis

The results of all the electrophoretic measurements are given in Table 1 and some of the electrophoretic patterns in Figure 1. In all cases, the patterns were reproducible and the areas of mobilities of the peaks were independent of the time of electrophoresis.

Initially, the α -keratose consists of one main electrophoretic component with about 14 per cent. of the material present as an ill-defined peak on the leading edge of the main boundary (Fig. 1 (a)). On the addition of small amounts

of NaDDS the descending boundary splits into two well-defined peaks (Fig. 1 (b)), while the ascending boundary remains unchanged. Such asymmetries between ascending and descending patterns are similar to those observed by Longworth and MacInnes (1942) for the interaction of protein and nucleic acid, and Smith and Briggs (1950) for the interaction of bovine serum albumin and methyl orange. These patterns are typical of cases where simple reversible interaction occurs between two species, and where the equilibrium involved in the formation

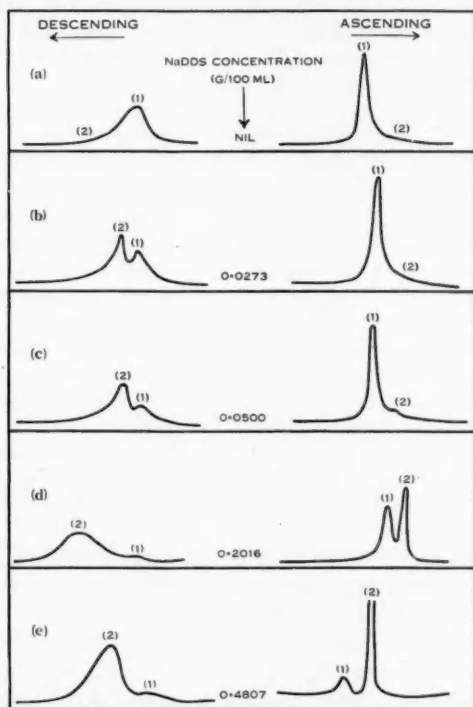


Fig. 1.—Electrophoresis patterns of NaDDS- α -keratose mixtures. Mobilities and relative amounts of components are given in Table 1.

of the complex is established rapidly in relation to the rate of electrophoretic separation.

If the interaction is of the type suggested then the slower peak on the descending side should represent a protein peak migrating with the mobility of unchanged α -keratose and the faster peak should represent a complex, since the effect of combination with DDS anion is to increase the net charge on the molecule. As seen from Table 1 the slower peak migrates in the mixture with a mobility of $4.77\text{--}5.32 \times 10^{-5}$ cm/sec/V/cm, as compared with 5.47×10^{-5}

cm/sec/V/cm for the original protein. This is considered to be satisfactory agreement considering the electrical heterogeneity of the protein (Fig. 1 (a)) and that in the protein-DDS mixture the protein is not the fastest peak and only the mobility of the fastest descending peak can be calculated accurately using the conductivity of the protein-DDS solution. The faster descending peak can justifiably be taken as due to a complex. The main ascending peak should correspond to the migration of a complex with increased mobility and if sufficient

TABLE 1

ELECTROPHORETIC DATA ON α -KERATOSE- α -NaDDS INTERACTION

Protein concentration was 1.04%. Electrophoresis was carried out at 1 °C, except those marked with *, which were done at 18 °C. All mobilities were calculated using the conductivity of the protein-detergent solution and are not corrected for changes in viscosity produced by the addition of NaDDS. For comparative purposes all mobilities are reduced to 0 °C

[NaDDS] (g/100 c.c.)	Total Number of Fringes	Relative Amounts of Components (No. of fringes)						Mobilities of Peaks at 0 °C (cm/sec/V/cm $\times 10^5$)			
		Descending			Ascending			Descending		Ascending	
		ϵ	1	2	δ	1	2	1	2	1	2
Nil	91	14	68	(9)†	23	59	(9)	5.47†	—	6.71	—
0.0133	91.5	14	52	25.5	24	58.5	(9)	5.18	6.40	6.57	—
0.0213	92	14	33	45	24	59	(9)	5.32	6.15	6.73	—
0.0273	92	15	31	46	24	60	(8)	4.82	5.62	6.49	—
0.0373	93	16	23	54	26	57	10	5.12	5.98	6.98	8.12
0.0500	92	15	23	54	23	59	10	5.03	5.90	7.11	8.09
0.1008	97	16	12.5	68.5	25.5	55	16.5	5.18	6.39	7.74	8.67
0.1496	100	16	11	73	25	53.5	21.5	4.77	6.71	8.26	9.03
0.2007*	102	17	9	76	27	55.5	19.5	4.85	7.67	8.98	9.74
0.2016	103	17	9	77	27	49	27	5.22	7.71	8.73	9.44
0.2504	104	16.5	7	80.5	28	46.5	29.5	—	8.27	9.23	9.97
0.3833*	110	18	11.5	80.5	29.5	19.5	61	5.97	9.16	9.60	10.68
0.4807*	116	20	14.5	81.5	31	17	68	8.13	8.72	8.34	10.74
0.7360*	132	25	10	97	37	21	74	—	9.52	11.87	12.89

† Figures in brackets represent incompletely resolved faster moving material present initially in α -keratose (see Fig. 1 (a)).

‡ Peak No. 1 on the descending side with mobility $4.8-5.4 \times 10^{-5}$ cm/sec/V/cm represents α -keratose. At concentrations of NaDDS of 0.2 g/100 ml the peak with this mobility disappears, and one main peak and about 15% of slower moving material are present both moving with mobility of DDS- α -keratose complexes.

free NaDDS is present a fast peak migrating with the mobility of the free DDS anion (or the micelle if the free NaDDS concentration is above the critical micelle concentration) should be observed. The main peak on the ascending side is assumed to be the complex peak, although there is little change in mobility until 0.0373 g of NaDDS has been added to the protein solution (Table 1) after which the mobility steadily increases with each addition of NaDDS. At low concentrations the amount of free NaDDS is too small to be detected optically.



but as its proportion is increased in the mixture a new faster moving peak does appear in the ascending side but this does not move with the mobility of free detergent (Fig. 1 (c)). The mobilities of both peaks on the ascending side increase with increasing concentration of NaDDS and the amount of material in the slower ascending boundary decreases, while that in the faster boundary increases. On the descending side with increase of NaDDS concentration the amount of free protein becomes too small to be seen and the protein-detergent complex consists of one main fairly spread out boundary together with a small slower-moving complex, the mobility of both increasing with increase of NaDDS concentration.

The protein shows a continuous uptake of DDS anion and does not exhibit the "all or none" characteristics shown in the combination of NaDDS with serum albumin (Putnam and Neurath 1945). Lundgren, Elam, and O'Connell (1943), also Pallansch and Briggs (1954) have shown that such an "all or none" change does not occur if the protein is previously denatured by heat. In the case of α -keratose the new peak which appears on the ascending side (Figs. 1 (c), 1 (d), 1 (e)) must correspond to the formation of a new complex. This new complex does not appear so early on the descending side but at the higher NaDDS concentrations two complexes are present as can be seen from the mobility data for the descending boundary (Table 1). The new peak on the ascending side appears at a point where the viscosity commences to fall rapidly on the addition of NaDDS and could be due to a configurational change in the protein allowing more DDS to be adsorbed. Such a mechanism has been postulated by Pallansch and Briggs (1954) to account for the appearance of a new complex in the combination of NaDDS with serum albumin. The viscosity and sedimentation data on the addition of NaDDS to α -keratose (Figs. 2 and 3) indicate both a disaggregation and a configurational change and it is not possible to say if either of these effects is responsible for the appearance of the new electrophoretic complex. There is no evidence from the electrophoresis patterns that the faster ascending boundary is associated with the known molecular heterogeneity of α -keratose (Alexander and Smith 1955; O'Donnell and Woods 1955), since the amount of protein in the slower ascending boundary continually decreases with addition of detergent although DDS is still being bound.

It has been shown that, for the combination of anionic detergents with other proteins, the positive sites on the molecule are essential for combination and also that detergent can combine in excess of this 1:1 combination with the positive sites. This secondary binding occurs by van der Waals' forces to these primarily bound detergent molecules. The following complexes of NaDDS with α -keratose can therefore be recognized: (i) those formed primarily by combination with the positive sites on the protein molecule and (ii) those formed by combination with DDS already bound to the protein. For small amounts of detergent, complexes of the first type will predominate and for larger amounts the second type. The second ascending peak (Figs. 1 (c), 1 (d), 1 (e)) which appears on electrophoresis with increasing NaDDS concentrations could correspond to the second type of complex. The amino acid analyses of Golden, Whitwell, and Mercer (1955) and Simmonds (1955) indicate that there would be

8 basic groups per 10^4 g in α -keratose. Dodecyl sulphate can combine with α -keratose to more than the equivalent of 3 moles DDS per basic group without free detergent appearing on electrophoresis. Such a complex containing 4 parts by weight of protein to 3 parts of NaDDS moves with a mobility less than that of a DDS micelle.* The electrophoretic behaviour is similar to that observed by Ward, High, and Lundgren (1946) in their study of a complex of chicken feather keratin (3 parts) with alkylbenzenesulphonate (2 parts). They found two main electrophoretic components and no free detergent, and therefore assumed that all the detergent was combined in the complex.

Cooling to 5 °C of a DDS- α -keratose complex containing more than 1 mole DDS per basic group, causes precipitation of NaDDS, leaving in solution a complex containing 1 mole DDS per basic group, suggesting that DDS above this level is loosely bound to the protein-detergent complex. Complete removal of DDS from the protein can be effected by prolonged dialysis against buffer or water and the recovered protein gives an electrophoretic pattern identical with the original α -keratose, the distribution and sedimentation coefficients of the ultracentrifuge components are the same, and the intrinsic viscosity is 0.287 as compared with 0.297 for the original protein. The removal of NaDDS by dialysis is difficult to reconcile with the stability of the complexes to electrophoresis.

Smith and Briggs (1950) and Alberty and Marvin (1950) have developed equations for the electrophoretic analysis of protein interactions similar to the case studied here and these equations should be applicable to the data at low NaDDS concentrations. The application of these equations requires a knowledge of the mobility of free DDS anion which is impossible to obtain electrophoretically since the critical micelle concentration in 0.2 ionic strength NaCl is 0.026 per cent. (Williams, Phillips, and Mysels 1955) and stable boundaries cannot be obtained in the electrophoresis apparatus below this concentration. The molecular heterogeneity of α -keratose (Alexander and Smith 1955; O'Donnell and Woods 1955) would in any case render such calculation doubtful. Similar considerations apply also to dialysis equilibrium studies in such a system and they were not therefore attempted.

(b) Viscosity and Sedimentation

Figure 2 shows the effect on the relative viscosity of α -keratose of the addition of increasing amounts of NaDDS. Small amounts cause a slight increase in viscosity, after which there is a rapid drop until approximately 2 moles NaDDS per positive group have been added when the viscosity starts to rise again. This rise in viscosity is greater than that due to the addition of NaDDS as is seen from the plot of relative viscosity of NaDDS in protein-free solutions. It is also seen from Figure 2 that the viscosity of α -keratose-NaDDS mixtures decreases with time after mixing. This time dependence is negligible after 18 hr.

* The mobility of the DDS micelle reduced to 0 °C and in 0.2 ionic strength NaCl calculated from the data of Stigter and Mysels (1955) was found to be 16.5×10^{-5} cm/sec/V/cm.

Figure 3 shows the sedimentation coefficient of the faster moving peak of α -keratose with increasing amounts of NaDDS. There is a decrease in S value

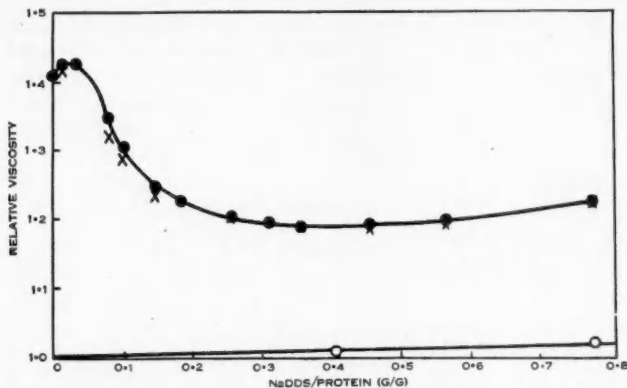


Fig. 2.—Viscosities relative to buffer (pH 6.7, $I=0.2$) of α -keratose (1.06%)-NaDDS mixtures.

- Readings made 1 hr after mixing.
- × Readings made 18 hr after mixing.
- Viscosity of pure NaDDS (abscissae is concentration in per cent.).

with increase of NaDDS up to 0.6 g NaDDS/g protein when the sedimentation coefficient reaches a constant value. The sedimentation diagram consists

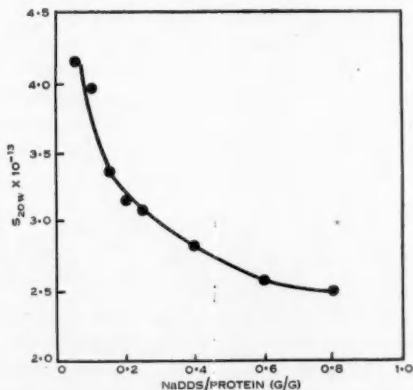


Fig. 3.—Sedimentation coefficients of α -keratose-NaDDS mixtures at pH 6.7, $I=0.2$.

initially of 2 peaks of S values 1.7 and 4.0 and is converted to a single peak with an S value between that of the initial peaks when 0.4 g DDS/g protein have been added. The protein-detergent complex is not homogeneous as there

is fairly rapid spreading of the sedimenting boundary with time, particularly at higher salt concentration.

The sequence of changes that take place can best be explained on the basis that α -keratose exists in solution as folded linear aggregates of monomer units. The increase in viscosity on addition of small amounts of NaDDS is due to expansion of the particle caused by the increase in net negative charge as the DDS anion combines with the positive sites on the protein molecule. Further combination of DDS leads to disaggregation with a sharp fall in viscosity and decrease in the sedimentation coefficient. There is a minimum in the viscosity at about 0.4 g DDS/g protein but not in the sedimentation coefficient. The rise in viscosity on increasing the concentration of NaDDS could be due to a further expansion of the α -keratose-DDS complex as the net charge increases.

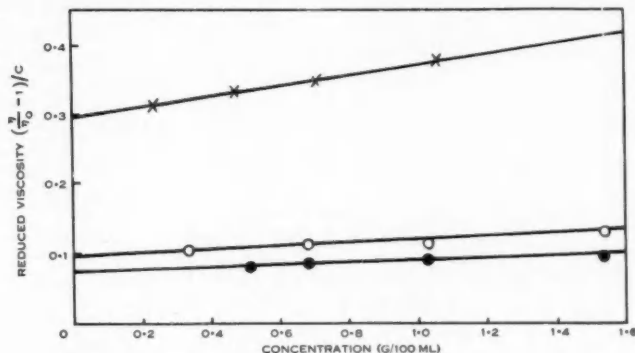


Fig. 4.—Reduced viscosity plotted against concentration of α -keratose, and a DDS- α -keratose complex, containing 2 moles DDS per basic group.

- × α -Keratose for pH 6.7, $I=0.2$.
- α -Keratose-DDS complex for pH 6.7, $I=0.2$.
- α -Keratose-DDS complex for pH 6.7, $I=1.0$.

(c) Size of the α -Keratose-DDS Complex

Estimates were made of the size of the complex containing 0.45 g NaDDS/g protein. This concentration is equivalent to 2 moles DDS anion per positive group on the protein and the complex shows minimum viscosity (Fig. 3) and a single peak in the ultracentrifuge (O'Donnell and Woods 1955). No free DDS anion can be detected on electrophoresis and 80 per cent. of the material is contained in one boundary. For viscosity and sedimentation experiments the concentration was taken as the total amount of NaDDS and α -keratose in the system, and it is necessary to assume that multiple dilutions do not affect the protein-detergent equilibria. This appears justified since the sedimentation coefficients and reduced viscosities when plotted against concentration extrapolate in a normal way and show no evidence of marked dissociation of the complex.

Figure 4 shows the reduced viscosities plotted against concentration for the complex at two different salt concentrations, and the same plot for the

original α -keratose solution. There is a small but definite effect of salt on the intrinsic viscosity of the complex. Similar effects in protein-detergent complexes have been described by other workers (Harrap and Schulman 1953). Figure 5 shows the reciprocal of the sedimentation coefficient-concentration graph for 0.2 and 1.0 ionic strength. At the higher ionic strength the complex appears much more heterogeneous.

From these data it is possible to make some estimate of the mean particle dimensions using the method described by Ogston (1953), whereby only data for sedimentation, velocity, and intrinsic viscosity are required. At 0.2 ionic strength $(d_s^1/dc) = 0.0413 \times 10^{13}$, $s_0 = 3.31 \times 10^{-13}$, and $[\eta] = 0.098$, giving an ellipticity of $J = 5$, a hydrodynamic volume $V^1 = 1.69$ c.c./g, and molecular weight $M = 70,500$. For the computation, \bar{V} for the complex was taken as 0.757,

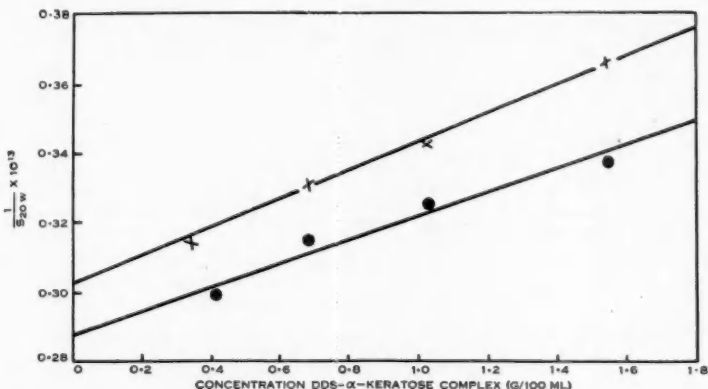


Fig. 5.—Reciprocal of sedimentation coefficient plotted against concentration for a DDS- α -keratose complex.

$\times I = 0.2$. $\bullet I = 1.0$.

being computed from the partial specific volumes of the protein (0.715) and sodium dodecyl sulphate (0.850). At 1.0 ionic strength $(d_s^1/dc) = 0.035 \times 10^{13}$, $s_0 = 3.48 \times 10^{-13}$, $[\eta] = 0.075$ giving J between 3 and 4, $V^1 = 1.64$, and $M = 68,400$.

The data indicate that the overall dimensions of the molecule are dependent on the salt concentration and, on the spheroidal model, the ellipticity lies between 3 and 5. The values obtained for V^1 , 1.67 c.c./g, are slightly more than twice the partial specific volume. The interpretation of the hydrodynamic quantities in terms of solvation has been recently discussed by Ogston (1955) and it would be reasonable to assume from the data that the complex is a moderately swollen coiled molecule of slight asymmetry.

The molecular weight of approximately 69,000 for the complex reduces to 48,000 when the amount of detergent combined with the protein is subtracted. This value is much higher than the figure 8000 obtained by Harrap (1955) using the surface balance technique and suggests that the complexing of DDS anion with α -keratose has only partially disaggregated the molecule. The results are comparable to those obtained by Ward, High, and Lundgren (1946) for the molecular size of a chicken feather alkylbenzenesulphonate complex containing 3 parts of protein to 2 parts detergent. They found the complex to be polydisperse with a weight average molecular weight of 75,000, the keratin portion of the complex being of molecular weight 40,000.

IV. ACKNOWLEDGMENTS

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PREPARATION OF ARYL ALDEHYDES FROM ARYL METHYL KETONES

By J. CYMERMAN-CRAIG,* J. W. LODER,* and B. MOORE*

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Summary

Arylglyoxylic acids can be readily obtained from solid aryl methyl ketones by permanganate oxidation of the latter in pyridine solution at 15 °C.

Decarboxylation of the glyoxylic acids in *NN*-dimethyl-*p*-toluidine affords good yields of the aryl aldehydes containing 1, 2, 3, and 4 aromatic rings.

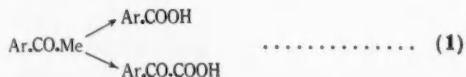
I. INTRODUCTION

While many aryl methyl ketones are readily accessible by the Friedel-Crafts reaction for ring systems containing up to five fused aromatic rings (for review, see Gore 1955), the preparation of the corresponding aryl aldehydes is attended with numerous difficulties.

Aryl aldehydes are obtainable by the decarboxylation of arylglyoxylic acids. These acids can be prepared by oxidation of *liquid* aryl methyl ketones (see, *inter alia*, Bouveault 1897*b*; Peter 1885) but the reaction is not applicable to solid aryl methyl ketones and this restricts the range of aryl aldehydes available by this method to one-ring compounds.

Popovici (1932) claimed that oxidation of methyl 2-naphthyl ketone at its m.p. (53 °C) gave 2-naphthylglyoxylic acid in 40 per cent. yield, accompanied by 2-naphthoic acid (cf. also Claus and Tersteegen 1890). The same author also reported oxidation during 15 days of a benzene solution of the ketone at room temperature. However, the product described by Popovici (1932) had m.p. 171 °C whereas 2-naphthylglyoxylic acid was found both by Blicke and Feldkamp (1944) and by the present authors to have m.p. 92 °C. It is possible that the product reported by Popovici (1932) contained appreciable amounts of 2-naphthoic acid (m.p. 182 °C).

Oxidation of aryl methyl ketones is known to proceed in two directions simultaneously (eqn. (1)) and in every case some of the carboxylic acid may be expected (see, *inter alia*, Bradley 1886).



The present work reports the facile preparation of arylglyoxylic acids in good yields from *solid* aryl methyl ketones by carrying out the oxidation in a water-soluble tertiary aromatic amine, pyridine being the solvent of choice.

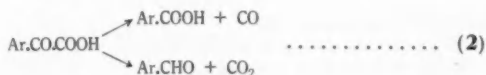
* Department of Organic Chemistry, University of Sydney.

Temperature variation was examined using methyl 2-naphthyl ketone and showed that 10–15 °C was the optimum temperature (Table 1) at which reaction was complete in 2 hours. By this means the arylglyoxylic acids in Table 1 have been obtained.

TABLE 1
PREPARATION OF ARYLGLYOXYLIC ACIDS

Aryl Methyl Ketone	Arylglyoxylic Acid (% yield)	Arylcarboxylic Acid (% yield)
2-Acetylbenzoic acid ..	Phthalonic acid, 45.5	c. 30
4 - Acetyl - 4' - methoxy- diphenyl	4 - Methoxydiphenyl - 4'-glyoxylic acid, 52	22
2-Acetylnaphthalene ..	2 - Naphthylglyoxylic acid : 34 (25–30 °C) 51 (10–15 °C) 49 (0–5 °C)	30 25 25
2-Acetylphenanthrene ..	2 - Phenanthrylgly- oxylic acid, 51	29
3-Acetylphenanthrene ..	3 - Phenanthrylgly- oxylic acid, 53	41
3-Acetylpyrene	3 - Pyrenylglyoxylic acid, 76	22

Thermal decomposition of arylglyoxylic acids is known to occur by two simultaneous routes (eqn. (2)) (Claisen 1877).



Hurd and Raterink (1934) carried out the reaction at 270 °C while Barger and Easson (1938) used acetic acid as solvent at 200 °C. Bouveault (1897a) and Barnes, Pierce, and Cochrane (1940) decarboxylated the Schiff's base formed by heating the keto acid with aniline, subsequently hydrolysing the product to the aldehyde. Bouveault (1898) showed that dimethylaniline could be used, and Guyot and Gry (1910) found that *NN*-dimethyl-*p*-toluidine was a more efficient reagent in one case, being effective even in catalytic quantity. For low-boiling aldehydes, the use of diphenylamine has been reported (Trister and Hibbert 1936).

Different methods of decarboxylation were investigated using 4-methoxydiphenyl-4'-glyoxylic acid. Attempted decarboxylation of the keto acid *in vacuo*

with or without a copper bronze catalyst resulted only in sublimation of unchanged material. Reaction of the keto acid with (i) aniline followed by acid hydrolysis, (ii) quinoline in presence of a copper catalyst, and (iii) dimethylaniline, all gave low yields of somewhat coloured aldehyde, while *NN*-dimethyl-*p*-toluidine gave a good yield of pure aldehyde.

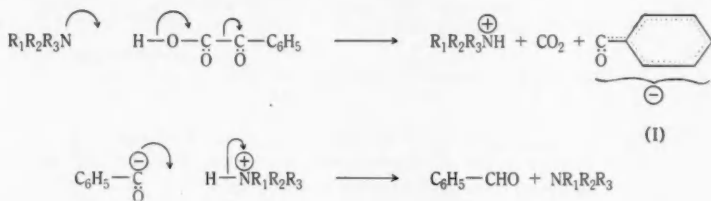


Fig. 1.—Postulated mechanism of decarboxylation of arylglyoxylic acids.

We also examined the effect of using tertiary amines of differing basic strengths as decarboxylating catalysts, and found (using 2-naphthylglyoxylic acid) that 2-naphthaldehyde was produced in 86, 84, and 81 per cent. yield respectively using *NN*-dimethyl-*p*-toluidine, *N*-ethylmorpholine, and *NN*-dimethylcyclohexylamine. The yields are substantially the same but the first substance was preferable as the two latter amines gave traces of gummy by-products.

TABLE 2
PREPARATION OF ARYL ALDEHYDES

Aldehyde	Yield (%)	Temperature (°C)
Phthalaldehydic acid	38	150
4-Methoxydiphenyl-4'-aldehyde ..	90	140-145
2-Naphthaldehyde	86	120
Phenanthrene-2-aldehyde	67	140-145
Phenanthrene-3-aldehyde	85	150
Pyrene-3-aldehyde	72	130

The reaction (Fig. 1) appears to be a base-catalysed elimination in which the base removes a proton from the acid, leaving an anion, which decarboxylates (either simultaneously or subsequently) by heterolysis of the carbon-carbon bond (cf. Brown 1951) to give a highly resonance-stabilized mesomeric anion (I), whose stabilization provides the driving force for the reaction.

The carbanion (I) then forms the aldehyde by a nucleophilic attack on the protonated tertiary amine. It has been shown (cf. *inter alia*, Brown and Hammick

1949) that the carboxyl group is usually in the anionic form before decarboxylation.

When the above arylglyoxylic acids, mixed with an equal volume of *NN*-dimethyl-*p*-toluidine, were kept at the lowest temperature at which a homogeneous solution could be obtained, until the evolution of carbon dioxide had ceased, good yields of the aldehydes were obtained for aromatic systems containing 1, 2, 3, and 4 benzene rings (Table 2).

II. EXPERIMENTAL

Analyses are by Miss B. Stevenson, University of Sydney.

(a) *Phthalonic Acid*.—A mixture of potassium hydroxide (1 g) in water (100 ml) and 2-acetylbenzoic acid (1.75 g) in pyridine (150 ml) was treated gradually over 2 hr with potassium permanganate (4.75 g) in water (400 ml) at 10–15 °C with stirring and cooling. After a further 30 min stirring, excess of permanganate was decomposed by addition of the minimum of solid sodium sulphite and the precipitated manganese dioxide filtered off. The filtrate was acidified with hydrochloric acid and the solution extracted continuously with ether for 6 hr. Distillation of the dried (Na_2SO_4) extracts left an oil (1.7 g) which crystallized on standing. Extraction of the crystals with chloroform gave (soluble portion) phthalonic acid (0.94 g, 45.5% yield), m.p. 142 °C, undepressed on admixture with authentic material.

The chloroform-insoluble material was phthalic acid (0.1 g, m.p. 190 °C) and removal of solvent from the chloroform mother liquors left an oil, which with 2,4-dinitrophenylhydrazine gave 0.05 g of the 2,4-dinitrophenylhydrazone (equivalent to a further 0.03 g of phthalonic acid).

(b) *2-Naphthylglyoxylic Acid*.—Solutions of 2-acetylnaphthalene (4.52 g) in pyridine (200 ml) and potassium hydroxide (2.5 g) in water (100 ml) were mixed and treated with potassium permanganate (13 g) in water (500 ml) at 10–15 °C over 2 hr with stirring. After a further 30 min stirring, excess permanganate was destroyed by addition of sodium sulphite, and the manganese dioxide filtered off and washed with hot water.

The filtrate was acidified with hydrochloric acid (10N) and the precipitate collected (A). The filtrate was extracted with ether giving an oil solidifying to 2-naphthylglyoxylic acid (2.72 g, 51% yield), crystallizing from light petroleum (b.p. 60–90 °C) as yellow cubes, m.p. 91–92 °C. Its 2,4-dinitrophenylhydrazone formed orange needles from ethanol, m.p. 219 °C (Found: C, 56.7; H, 3.3%. Calc. for $\text{C}_{18}\text{H}_{12}\text{O}_4\text{N}_4$: C, 56.8; H, 3.2%).

The precipitate (A) was 2-naphthoic acid (1.42 g, 25% yield), m.p. and mixed m.p. 180–182 °C.

(c) *4-Methoxydiphenyl-4'-glyoxylic Acid*.—A mixture of 4-acetyl-4'-methoxydiphenyl (4.52 g) in pyridine (180 ml) and potassium hydroxide (3 g) in water (100 ml) was oxidized with potassium permanganate (10.5 g) in water (500 ml). Acidification of the alkaline solution after removal of manganese dioxide gave a precipitate which was filtered and dissolved in hot dilute potassium hydroxide solution.

On cooling, a potassium salt crystallized which was filtered off (A), dissolved in hot water, and acidified to give 4-methoxydiphenyl-4'-glyoxylic acid (2.65 g, 52% yield), crystallizing from benzene as yellow needles, m.p. 165–166 °C (Found: C, 70.1; H, 4.6%. Calc. for $\text{C}_{15}\text{H}_{12}\text{O}_4$: C, 70.3; H, 4.2%).

The 2,4-dinitrophenylhydrazone crystallized from aqueous acetone as golden-yellow needles, m.p. 210–211 °C (decomp.) (Found: C, 57.4; H, 3.8%. Calc. for $\text{C}_{21}\text{H}_{14}\text{O}_7\text{N}_4$: C, 57.8; H, 3.7%).

Acidification of the alkaline filtrate from A gave 4-methoxydiphenyl-4'-carboxylic acid (0.99 g, 22% yield), m.p. 250 °C. Johnson, Gutsche, and Offenbauer (1946) give m.p. 248–249 °C.

(d) *2-Phenanthrylglyoxylic Acid*.—Oxidation of 2-acetylphenanthrene (5.25 g) in pyridine (500 ml) with potassium hydroxide (3 g) in water (100 ml) and potassium permanganate (12.5 g) in water (400 ml) was slow at 10–15 °C due to the low solubility of the ketone, and the temperature

was raised to 30 °C. After stirring for 2 hr, the alkaline solution, after removal of manganese dioxide, was acidified giving phenanthrene-2-carboxylic acid (1.54 g, 29% yield), m.p. 256–258 °C. Mosettig and van de Kamp (1930) give m.p. 258.5–260 °C.

Ether extraction of the aqueous filtrate gave 2-phenanthrylglyoxylic acid (3.01 g, 51% yield), m.p. 140–145 °C. The semicarbazone crystallized from 2-ethoxyethanol as yellow needles m.p. 234 °C (Found: C, 66.2; H, 4.6%. Calc. for $C_{17}H_{13}O_2N_3$: C, 66.4; H, 4.3%).

(e) *3-Phenanthrylglyoxylic Acid*.—Preparation from 3-acetylphenanthrene (4.4 g) in pyridine (150 ml), potassium hydroxide (2.5 g) in water (100 ml), and potassium permanganate (10 g) in water (500 ml) gave, on acidification of the filtered reaction mixture, phenanthrene-3-carboxylic acid (1.81 g, 41% yield), crystallizing from acetic acid as needles, m.p. 268–270 °C. Mosettig and van de Kamp (1930) give m.p. 270 °C. Ether extraction of the filtrate gave 3-phenanthrylglyoxylic acid (2.66 g, 53% yield), m.p. 140–145 °C, characterized as the semicarbazone, m.p. 180–181 °C, from aqueous ethanol (Found: C, 64.3; H, 4.2%. Calc. for $C_{17}H_{13}O_2N_3 \cdot 0.5H_2O$: C, 64.3; H, 4.4%).

(f) *3-Pyrenylglyoxylic Acid*.—Reaction of 3-acetylpyrene (4.65 g) in pyridine (200 ml), potassium hydroxide (2.5 g) in water (100 ml), and potassium permanganate (9.5 g) in water (400 ml) gave pyrene-3-carboxylic acid (1.06 g, 22% yield), m.p. 266 °C from chlorobenzene (Vollmann *et al.* (1937) give m.p. 274 °C) and 3-pyrenylglyoxylic acid (3.98 g, 76% yield), crystallizing from ethanol, m.p. 170–172 °C. Its 2,4-dinitrophenylhydrazone formed dark red crystals of a hemihydrate from aqueous ethanol, m.p. 220–221 °C (Found: C, 62.4; H, 3.3%. Calc. for $C_{24}H_{18}O_6N_4 \cdot 0.5H_2O$: C, 62.2; H, 3.3%).

(g) *Phthalaldehydic Acid*.—Phthalonic acid (3 g) and *NN*-dimethyl-*p*-toluidine (3 ml) were heated together until homogeneous (160 °C) and kept at this temperature till evolution of carbon dioxide ceased (1.5 hr). The cooled solution was taken up in ether, washed with dilute hydrochloric acid, and distilled giving an oil (2.25 g) affording the 2,4-dinitrophenylhydrazone of phthalaldehydic acid (1.93 g, corresponding to 0.88 g or 38% yield of the aldehyde), crystallizing from ethanol as orange needles, m.p. 247–248 °C undepressed on admixture with an authentic specimen (Found: C, 50.8; H, 3.3%. Calc. for $C_{14}H_{10}O_6N_4$: C, 50.9; H, 3.1%).

(h) *2-Naphthaldehyde*.—Reaction of 2-naphthylglyoxylic acid (2 g) and *NN*-dimethyl-*p*-toluidine (2 ml) at 120 °C gave 2-naphthaldehyde (1.34 g, 86% yield) as yellow crystals from *n*-hexane, m.p. 59–60 °C. Krollpfeiffer (1923) gives m.p. 60.5 °C. The semicarbazone had m.p. 245–247 °C. Monier-Williams (1906) gives m.p. 245 °C.

(i) *4-Methoxydiphenyl-4'-aldehyde*.—4-Methoxydiphenyl-4'-glyoxylic acid (2 g) and *NN*-dimethyl-*p*-toluidine (2 ml) at 140–145 °C gave 4-methoxydiphenyl-4'-aldehyde (1.5 g, 90% yield), crystallizing from light petroleum (b.p. 90–100 °C) as white needles, m.p. 101.5–102 °C undepressed on admixture with the material, m.p. 101.5–102 °C, of Cymerman-Craig and Loder (1956) obtained by the McFadyen-Stevens reaction.

(j) *Phenanthrene-2-aldehyde*.—Decarboxylation of 2-phenanthrylglyoxylic acid (2 g) with *NN*-dimethyl-*p*-toluidine (2 ml) at 140–145 °C gave phenanthrene-2-aldehyde (1.1 g, 67%), crystallizing from *n*-hexane as needles, m.p. 58–59 °C. Mosettig and van de Kamp (1933) give m.p. 59–59.5 °C. The semicarbazone formed needles from aqueous ethanol, m.p. 277–278 °C. Mosettig and van de Kamp (1933) give m.p. 281–282 °C.

(k) *Phenanthrene-3-aldehyde*.—Decarboxylation of 3-phenanthrylglyoxylic acid (1 g) at 150 °C as described in (j) gave phenanthrene-3-aldehyde (0.7 g, 85% yield), m.p. 78–79 °C. Mosettig and van de Kamp (1933) give m.p. 79.5–80 °C.

The semicarbazone crystallized from ethanol as white needles, m.p. 219–220 °C (Found: C, 73.3; H, 5.1%. Calc. for $C_{16}H_{12}ON_3$: C, 73.0; H, 5.0%). Mosettig and van de Kamp (1933) give m.p. 274–275 °C for this compound.

(l) *Pyrene-3-aldehyde*.—3-Pyrenylglyoxylic acid (1 g) was decarboxylated at 130 °C during 1 hr by the method described in (h), giving pyrene-3-aldehyde (0.6 g, 72% yield), crystallizing from aqueous ethanol as orange plates, m.p. 126 °C. Vollmann *et al.* (1937) give m.p. 126 °C. The phenylhydrazone formed yellow needles from aqueous ethanol, m.p. 200–201 °C. Vollmann *et al.* (1937) give m.p. 201–202 °C.

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METHYLSTEROIDS

II. 3 β -HYDROXY-4,4,14-TRIMETHYLalloPREGNAN-20-ONE, A PROGESTERONE ANALOGUE

By C. S. BARNES*

[Manuscript received November 11, 1955]

Summary

The title compound has been prepared from lanosterol and may have progestational activity.

I. INTRODUCTION

From the observation of Voser *et al.* (1953) and Ruzicka (1953) that the hormone homologue 11-oxo-14-methylprogesterone (I) has comparable activity to the true hormone it is apparent that the 14-methyl-group has no adverse effect on hormonal properties. Activity might also be expected from homologues of other hormones derived from lanosterol (II). Of these the most attractive would be homologues of the adrenocorticoids as the 11-oxo-group is readily introduced in the lanosterol series. The previously mentioned 11-oxo-14-methylprogesterone (I) could be an intermediate in such a synthesis.

An important operation in preparing such compounds is the conversion of the triterpenoid ring A of lanosterol to one containing the $\alpha\beta$ -unsaturated ketone system as in I, which is regarded as essential for maximum activity in the non-aromatic steroidal hormones. Although an ingenious method for this conversion has been devised by Voser *et al.* (1952) it remains a relatively long and low-yielding process.

It seemed desirable to know whether this process is necessary with lanosterol, for if it were not, lanosterol would be more favourably placed for conversion to biologically active material.

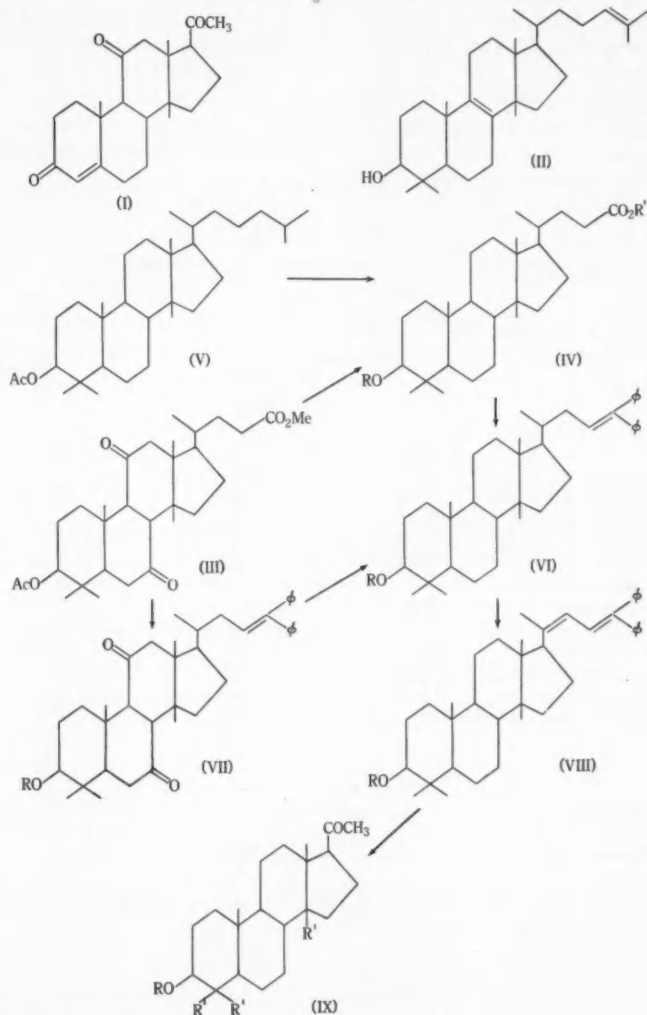
Langdon and Bloch (1952) have shown that cholesterol can be biosynthesized from the open-chain triterpene, squalene. While the detailed mechanism is not certain (for review, see Cornforth 1954) it is probable that a cyclization step is involved which results in the formation of a polycyclic structure having a *gem*-dimethyl group on ring A. The steroidal ring A is then formed by subsequent methyl eliminations.

We are grateful to Dr. T. R. Forbes of Yale University, who found compound IX (R=H) to be inactive in the bioassay for progesterone (Hooker and Forbes 1947). This would be expected of a prohormone.

Compounds similar to a known hormone in rings B, C, and D with their substituents, but retaining the triterpenoid type ring A, should be readily

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obtained from lanosterol. These might then act as prohormones since *in vivo* changes of ring A could result in conversion to active compounds.



A progesterone analogue seemed most suitable as a test substance because of the rigid structural requirements for progestational activity. Thus the alcohol (IX ; $\text{R}=\text{R}'=\text{H}$), having a saturated ring system, is inactive (Burger 1951). As a model the corresponding trimethyl compound (IX ; $\text{R}=\text{H}$, $\text{R}'=\text{Me}$) was prepared from lanosterol.

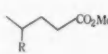
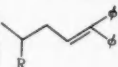
II. 3 β -HYDROXY-4,4,14-TRIMETHYLalloPREGNAN-20-ONE

For the preparation of the hydroxy acid (IV ; R=R'=H) the dioxoester (III) of Voser, Jeger, and Ruzicka (1952) was reduced by the modified Wolff-Kishner method of Barton, Ives, and Thomas (1955) to the sparingly soluble hydroxy acid (IV ; R=R'=H), which was characterized by its acetate and benzoate methyl esters.

Alternatively the acetate methyl ester (IV ; R=Ac, R'=Me) was obtained in small yield from the methylated acid fraction after vigorous chromic acid oxidation of lanostanyl acetate (V).

TABLE I

MOLECULAR ROTATION DIFFERENCES ON SIDE-CHAIN DEGRADATION

R	[M] _D in Chloroform			Δ ₁ [*]	Δ ₂	Ref.
	C ₁₇ Side-chain					
			$\begin{array}{c} \text{CH}_3\text{C}=\text{O} \\ \\ \text{R} \end{array}$			
3β-Acetoxy-4,4,14-trimethyl-androstane	+181°	+314°	+362°	+133°	+181°	†
3β-Hydroxy-11-oxo-4,4,14-trimethylandrostane	+250	+397	+410	+147	+160	‡
3β-Acetoxyandrostane	+48	+183	+277	+135	+229	

$$^* \Delta_1 = [\text{M}]_D \begin{array}{c} \text{CH}_3 \\ | \\ \text{CH} \\ | \\ \text{R} \end{array} \text{CH}=\text{CH}-\text{CO}_2\text{Me} - [\text{M}]_D \begin{array}{c} \text{CH}_3 \\ | \\ \text{CH} \\ | \\ \text{R} \end{array} \text{CH}_2\text{CH}_2\text{CO}_2\text{Me}$$

$$\Delta_2 = [\text{M}]_D \begin{array}{c} \text{CH}_3\text{C}=\text{O} \\ | \\ \text{R} \end{array} - [\text{M}]_D \begin{array}{c} \text{CH}_3 \\ | \\ \text{CH} \\ | \\ \text{R} \end{array} \text{CH}_2\text{CH}_2\text{CO}_2\text{Me}$$

† Experimental.

‡ Voser *et al.* (1952).

|| Meystre and Miescher (1946); Barton and Brooks (1949); Shoppee (1949).

Subsequent degradation of the side chain followed closely the well-known method of Meystre *et al.* (1944).

The action of phenylmagnesium bromide on the ester (IV ; R=Ac, R'=Me) followed by dehydration of the carbinol with acetic anhydride gave the diphenylethylene (VI ; R=Ac).

For confirmation of the structure, VI was prepared by an alternative route. The action of phenylmagnesium bromide on the dioxoester (III) followed by dehydration with acetic anhydride, gave the dioxodiphenylethylene (VII ; R=Ac). Vigorous Wolff-Kishner reduction (Barton, Ives, and Thomas 1955) of the carbonyls then gave VI.

From VI ($R=Ac$), the diphenylbutadiene (VIII; $R=Ac$) was formed by a sunlight catalysed dehydrogenation with *N*-bromosuccinimide.

The desired oxo-alcohol (IX; $R=H$, $R'=Me$) was then obtained by oxidative removal of the side chain of VIII ($R=Ac$) with chromic acid followed by hydrolysis.

Structures of the unsaturated intermediates were confirmed by their ultra-violet absorption spectra; molecular rotation differences (Table 1) also support the assigned structures.

In the first instance IX ($R=H$, $R'=Me$) was tested by Dr. B. Hudson. When, in ethyl oleate solution, it was injected at the rate of 0.3 mg per day for 5 days into 5 castrated oestrogen-treated female rats, it produced an effect on the uterine endometrium of each animal similar to that of progesterone (0.2 mg per day).

Further assays are in progress. Recently, Bloch and Tchen (1955) have established that lanosterol is an intermediate in the synthesis by rat liver preparations of cholesterol from squalene.

III. EXPERIMENTAL

(a) *General*.—As in Part I of this series (Barnes and Palmer 1956).

(b) *3 β -Hydroxy-25,26,27-trisnorlanostan-24-oic Acid (IV; $R=R'=H$) and Derivatives*.—(i) 3 β -Acetoxy-7,11-dioxo-25,26,27-trisnorlanostan-24-oic acid methyl ester (III) (15 g) was added to the product from sodium (10 g) and diethylene glycol (400 ml) and heated until dissolved. Anhydrous hydrazine (30 ml) was added and the solution heated to 180°C for 18 hr.

Working up in the usual way gave a neutral fraction (5 g). Acidification of the aqueous alkaline solution precipitated the free acid, which was sparingly soluble in the common extracting solvents. Filtration and methylation (diazomethane) gave the *hydroxy methyl ester* (IV; $R=H$, $R'=Me$), which crystallized from light petroleum having m.p. 177–180°C, $[\alpha]_D^{+30}$ (c, 1.6) (Found: C, 77.9; H, 11.3; O, 11.4%. Calc. for $C_{28}H_{48}O_3$: C, 77.7; H, 11.2; O, 11.1%).

Acetylation (acetic anhydride/pyridine on the steam-bath) gave the *acetate methyl ester* (IV; $R=Ac$, $R'=Me$), which crystallized from chloroform-methanol, m.p. 196–197°C, $[\alpha]_D^{+38}$ (c, 1.5) (Found: C, 76.2; H, 10.6; O, 13.5%. Calc. for $C_{30}H_{50}O_4$: C, 75.9; H, 10.6; O, 13.5%).

Benzoylation of the hydroxy methyl ester (benzoyl chloride/pyridine on the steam-bath) gave the *benzoate methyl ester* (IV; $R=Bz$, $R'=Me$), which crystallized from light petroleum, m.p. 206–207°C, λ_{max} 230 m μ , ϵ 14000 (Found: C, 78.3; H, 9.8%. Calc. for $C_{35}H_{58}O_4$: C, 78.3; H, 9.8%).

(ii) A solution of chromium trioxide (30 g) in water (50 ml), acetic acid (150 ml), and sulphuric acid (35 ml) was run slowly into a solution of lanostanyl acetate (V) (11 g) in methylene chloride (10 ml), acetic acid (300 ml), and acetic anhydride (15 ml), with stirring and cooling to maintain a temperature of 30–35°C. After standing overnight at room temperature the mixture was worked up in the usual way to give an acid (6 g) and neutral (4 g) fraction.

Chromatography of the neutral fraction gave as the only crystalline product a *ketone*, crystallizing from methanol, m.p. 184–185°C (Found: C, 78.9; H, 10.8%. Calc. for $C_{27}H_{48}O_2$: C, 78.8; H, 11.1%). This is possibly 25-oxo-27-norlanostan-3 β -yl acetate. The *derived 2,4-dinitrophenylhydrazones* crystallized from chloroform, m.p. 234–236°C (Found: C, 68.2; H, 8.5; O, 15.0; N, 8.9%. Calc. for $C_{27}H_{48}O_6N_4$: C, 68.1; H, 8.6; O, 14.7; N, 8.6%).

Chromatography of the methylated acid fraction (by A. Palmer) over alumina gave in the benzene eluted fraction the *acetate methyl ester* (IV; $R=Ac$; $R'=Me$) crystallized from chloroform-methanol, m.p. 195–196°C undepressed on admixture with that previously obtained.

Hydrolysis and methylation gave the hydroxy methyl ester, m.p. 175–177 °C, undepressed on admixture with that previously obtained.

(c) *7,11-Dioxo-24,24-diphenyl-25,26,27-trisnorlanost-23-en-3 β -ol* (VII; R=H) and *Derivatives*.—The dioxomethyl ester (III) (20 g) in benzene (400 ml) was added to a solution of phenylmagnesium bromide (magnesium (15 g) and bromobenzene (75 g) in ether (300 ml)). Some ether (200 ml) was distilled, the remaining solution refluxed overnight, and poured onto ice (500 g) and ammonium chloride (45 g). After steam distilling the diphenyl the ether-soluble material was heated 1 hr in refluxing acetic anhydride (300 ml) and filtered through alumina from a light petroleum solution. Light petroleum eluted the *acetate* (VII; R=Ac), which crystallized from chloroform-methanol, m.p. 221–222 °C, $[\alpha]_D^{+68}$ (c, 1.2), λ_{\max} 215, 250 m μ , ϵ 14000, 17600 (Found: C, 79.8, 79.8; H, 8.9, 8.5%. Calc. for $C_{41}H_{52}O_4 \cdot 0.5CH_3OH$: C, 79.8; H, 8.7%).

Elution with ether gave a fraction which on crystallization from chloroform-methanol had m.p. 225–227 °C. This is evidently *7,11-dioxo-24,24-diphenyl-25,26,27-trisnorlanostan-3,24-diol-3-acetate*, since on treatment with iodine in refluxing benzene the *acetate* (VII; R=Ac) was obtained.

Hydrolysis of the *acetate* (VII; R=Ac) (500 mg) with methanolic potassium hydroxide (50 ml; 5%) for 45 min under reflux gave the derived *alcohol* (VII; R=H) which crystallized from chloroform-methanol to have m.p. 275–277 °C, $[\alpha]_D^{+66}$ (c, 1.2), λ_{\max} 222–226, 250 m μ , ϵ 13000, 15600 (Found: C, 82.5; H, 8.7; O, 8.5%. Calc. for $C_{39}H_{50}O_3$: C, 82.6; H, 8.9; O, 8.5%).

Benzoylation (benzoyl chloride/pyridine on the steam-bath) gave the *benzoate* (VII; R=Bz)* which crystallized from chloroform-methanol, m.p. 251–252 °C, λ_{\max} 225, 228 m μ , ϵ 24500, 24000, λ_{inflex} 230, 248 m μ , ϵ 24000, 17000 (Found: C, 82.1; H, 8.2; O, 9.7%. Calc. for $C_{48}H_{54}O_4$: C, 82.3; H, 8.1; O, 9.5%).

(d) *24,24-Diphenyl-25,26,27-trisnorlanost-23-en-3 β -ol* (VI; R=H) and *Derivatives*.—

(i) The *acetate methyl ester* (IV; R=Ac, R'=Me) (9 g) in benzene (400 ml) was added to a solution of phenylmagnesium bromide (bromobenzene (50 g) and magnesium (10 g) in ether (400 ml) and the ether (300 ml) distilled off. The remaining benzene solution was refluxed overnight, poured onto ice and ammonium chloride, and the ether-soluble material steam distilled to remove diphenyl. The residue, on treatment with refluxing acetic anhydride (300 ml) for 1 hr and cooling, gave the *acetate* (VI; R=Ac) which crystallized from chloroform-light petroleum, m.p. 243–246 °C, $[\alpha]_D^{+54}$ (c, 2.0), λ_{\max} 250 m μ , ϵ 13000 (Found: C, 84.5; H, 9.7; O, 5.4%. Calc. for $C_{41}H_{54}O_2$: C, 84.8; H, 9.7; O, 5.5%).

(ii) The *acetate dioxodiphenylethylene* (VII; R=Ac) (13 g) was added to a solution of sodium (15 g) in diethylene glycol (700 ml) and anhydrous hydrazine (25 ml) added. After heating overnight at 190 °C the reaction mixture was diluted with water and methanol and the precipitated product recovered by centrifuging and filtration. Recrystallized from chloroform-methanol it gave the *alcohol* (VI; R=H), m.p. 236–238 °C, λ_{\max} 220, 250 m μ , ϵ 12000, 14000 (Found: C, 87.0; H, 10.1%. Calc. for $C_{38}H_{48}O$: C, 86.9; H, 10.1%).

Acetylation with refluxing acetic anhydride gave the *acetate* (VI; R=Ac), m.p. 235–237 °C undepressed on admixture with that obtained previously, but depressing 15 °C with the parent *alcohol*.

(e) *24,24-Diphenyl-25,26,27-trisnorlanosta-20(22),23-dien-3 β -ol* (VIII; R=H) and *Derivatives*.—To a solution of the diphenylethylene (VI; R=Ac) (300 mg) in carbon tetrachloride (20 ml) was added *N*-bromosuccinimide (120 mg; 20% excess). The solution was refluxed in bright sunlight for 15 min, cooled, and filtered. After adding acetic acid (5 ml) to the filtrate the solvent was slowly distilled for 2 hr, when the residue was worked up in the usual way.

* The absorption maximum and high m.p. recorded by McGhie *et al.* (1951) for this compound suggests they may have had the *alcohol* (VII; R=H) formed by action of phenylmagnesium bromide on the *3-benzoate* of *3-benzoyloxy-7,11-dioxo-25,26,27-trisnorlanostan-24-oic acid methyl ester*.

Crystallization of the product from chloroform-methanol gave the *acetate* (VIII; R=Ac) which had m.p. 237–238°C, $[\alpha]_D^{+76}$ (c, 1.5), $+76^\circ$ (c, 1.1), λ_{\max} 305 m μ , ϵ 27500 (Found: C, 85.0; H, 9.6; O, 5.3%. Calc. for $C_{41}H_{54}O_2$: C, 85.0; H, 9.4; O, 5.6%).

Hydrolysis in the usual way (methanolic potassium hydroxide) gave the *alcohol* (VIII; R=H), which crystallized from chloroform-methanol, m.p. 232–234°C, $[\alpha]_D^{+55}$ (c, 1.0), $+53^\circ$ (c, 1.2), λ_{\max} 305 m μ , ϵ 28500 (Found: C, 87.3; H, 9.8%. Calc. for $C_{39}H_{52}O$: C, 87.3; H, 9.8%).

(f) β -Hydroxy-4,4,14-trimethylallopregnan-20-one (IX; R=H, R'=Me) and Derivatives.—To a solution of the diphenylbutadiene (VIII; R=Ac) (1 g) in chloroform (20 ml) and acetic acid (30 ml) at room temperature, was added a solution of chromium trioxide (1 g) in water (5 ml) and acetic acid (10 ml). After standing 40 min the solution was worked up in the usual way. Crystallized from methanol the resulting *acetate ketone* (IX; R=Ac, R'=Me) had m.p. 210–211°C, $[\alpha]_D^{+90}$ (c, 1.4) (Found: C, 77.3; H, 10.7; O, 12.2%. Calc. for $C_{28}H_{42}O_3$: C, 77.6; H, 10.5; O, 11.9%).

Hydrolysis in the usual way (methanolic potassium hydroxide) gave the *hydroxy ketone* (IX; R=H, R'=Me), which crystallized from methanol, m.p. 256–258°C, $[\alpha]_D^{+87}$ (c, 0.8) (Found: C, 79.8; H, 11.2%. Calc. for $C_{24}H_{40}O_2$: C, 79.9; H, 11.2%).

The hydroxy ketone (IX; R=H, R'=Me) (10 mg) with 2,4-dinitrophenylhydrazine (10 mg) in ethanol (10 ml) with 1 drop of hydrochloric acid gave on warming the derived 2,4-dinitrophenylhydrazone, m.p. 270–272°C (Found: N, 9.9%. Calc. for $C_{30}H_{44}O_5N_4$: N, 10.3%).

IV. ACKNOWLEDGMENTS

Thanks are due to Dr. B. Hudson of the Baker Medical Research Institute, Melbourne, who performed the biological test.

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LOGANIN

I. SOME OBSERVATIONS ON THE STRUCTURE

By A. J. BIRCH* and ESTELLE SMITH†

[Manuscript received December 16, 1955]

Summary

The glucoside, loganin, is shown to contain the groupings $C-CH_3$, $C=C-C=O$, and CO_2CH_3 , and several new derivatives are described. As a working hypothesis formula I is advanced.

I. INTRODUCTION

The glucoside, loganin, from *Strychnos* species, a member of the family Loganiaceae, and from *Menyanthes trifoliata* Linn., belonging to the family Gentianaceae, was assigned the formula $C_{17}H_{26}O_{10}$ by Merz and Krebs (1937) on the basis of molecular weight determinations and numerous analyses. It was considered to be a lactone containing one methoxyl and five hydroxyl groups; 1 mole of glucose is formed by hydrolysis with emulsin. The aglycone, loganetin, is very unstable and has not been obtained crystalline, but a crystalline di-*p*-nitrobenzoate and mono- and ditriphenylmethyl ethers were formed, corresponding to the expected $C_{11}H_{16}O_5$ with two hydroxyl groups. Hydrogenation of loganin could not be accomplished, but loganetin slowly took up 1 mole of hydrogen. A partial structure put forward by Merz and Krebs (1937) can bear no relation to the true structure in view of the results given in the present paper.

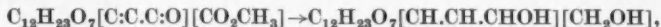
II. THE CARBONYL GROUP

Merz and Krebs (1937) publish an ultraviolet absorption curve which immediately suggests the presence of an $\alpha\beta$ -unsaturated ketone grouping; we have confirmed the presence of a band at λ_{\max} 242 m μ ; $\log \epsilon_{\max}$ 3.44. The infra-red spectrum has two bands which might correspond to a carbonyl group: one at 1708 cm^{-1} , the other at 1648 cm^{-1} . The former might appear to correspond to a saturated unstrained ketone, but the sum of the evidence seems to exclude the presence of such a group. The interpretation which we prefer is to regard the 1708 cm^{-1} band as due to an unsaturated ketone group in a five-membered ring, and that at 1648 cm^{-1} to a double bond conjugated with it. The lack of formation of formaldehyde on ozonolysis seems to exclude the presence of $C=CH_2$ which might have produced the latter band. Loganin was found to give very slowly an insoluble 2,4-dinitrophenylhydrazone.

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Reduction of loganin with sodium and ethanol in liquid ammonia, followed by the action of acetic anhydride, gave a crystalline product analysing for $C_{28}H_{42}O_{15}$, containing six acetyl groups. This corresponds to the change due to reduction:



with acetylation of six of the seven hydroxyl groups formed.

The product showed no selective absorption in the region 220–300 $m\mu$. The resistance to esterification of one hydroxyl group would be explicable on the basis of steric hindrance, since the keto-group of loganin is hindered and a hydroxyl group produced by its reduction would also be hindered.

III. THE ESTER GROUP

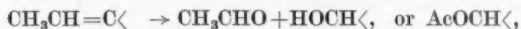
Merz and Krebs (1937) considered loganin to be a lactone, but with the recognition of the presence of a carbonyl group this formulation becomes impossible. It would require the presence of 5-OH (4 in the sugar); $-OCH_3$; $-COO-$; $C=O$ and 2-O (1 glycosidic, 1 in the sugar ring), that is, eleven oxygens. The only obvious solution to the difficulty is to assume that an oxygen is common to two of the above groups probably as $-CO_2CH_3$. This assumption is supported by the presence of a band at 1738 cm^{-1} and was confirmed by mild alkaline hydrolysis. The volatile portion gave the test of Denigès (1910) for methanol, and an acid (loganic acid) was obtained which could not be crystallized, but which gave rise to a penta-acetyl derivative $C_{16}H_{19}O_5(O_2CCH_3)_5$, m.p. 98 and 158°C (dimorphous). Diazomethane on this acetyl derivative regenerated penta-acetyl-loganin, m.p. 132°C , of unchanged optical rotation. The sodium reduction above also supports the presence of CO_2CH_3 . The ready hydrolysis of loganin shows that the ester group is not sterically hindered; moreover the compound cannot be a β -keto-ester because penta-acetyl-loganic acid is stable at 100°C . The methoxyl is retained in the 2,4-dinitrophenylhydrazone which cannot therefore be a dinitrophenylhydrazide, or be formed from an enol methyl ether.

IV. GENERAL OBSERVATIONS ON THE STRUCTURE

Loganin contains one $C-CH_3$ according to a Kuhn-Roth determination. The infra-red spectrum has a band at 1382 cm^{-1} which is unsplit, consequently the presence of a *gem*-dimethyl group is unlikely. A partial formula at this stage is $[C_5H_9][CH_3][C:C:C:O][CO_2CH_3][OH][OC_6H_{11}O_5]$, one carbon ring, probably five membered, being present. The position of the ultraviolet absorption maximum (242 $m\mu$) indicates that the double bond is probably disubstituted and exocyclic (calc. 242 $m\mu$) or possibly trisubstituted (calc. 249 $m\mu$) (Woodward 1942; Fieser and Fieser 1949).

Oxidation of loganin has so far given only formic acid and acetic acid (Merz and Krebs 1937). We have now examined the ozonolysis of penta-acetyl-loganin, and as a volatile product acetaldehyde was recognized as its 2,4-dinitrophenylhydrazone. Two other crystalline compounds were obtained from different experiments: A, m.p. 60°C , and B, m.p. 155°C , both of which contained a methoxyl group and apparently the tetra-acetylglucose residue. These

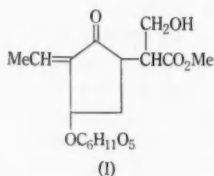
compounds were not soluble in sodium carbonate solution, gave no colour with ferric chloride, and did not give any isolable product with 2,4-dinitrophenylhydrazine and showed no selective absorption in the region 220–300 μ . The compounds may be isomeric, and analytical figures correspond possibly to $C_{26}H_{34}O_{16}$ or $C_{27}H_{36}O_{17}$, which could be produced by the reactions



respectively. Penta-acetyl β -glucose was obtained after reacetylation of the mother liquor from the crystallization of the ozonolysis products. Heating compound B with acetic anhydride gave an uncrystallizable gum.

Titration of loganin with periodic acid gave no useful results: 2 moles were consumed after 1.5 hr, probably by the sugar residue, but slow uptake continued to about 5 moles after 4 days.

When more material becomes available we hope to investigate further the oxidation and reduction products described. In the meantime we suggest formula I, which contains an isoprenoid skeleton, as a working hypothesis.



V. EXPERIMENTAL

The loganin used in this work was isolated from *Strychnos lucida* R.Br. (Anet, Hughes, and Ritchie 1953) and kindly presented to us by Dr. G. K. Hughes and Dr. E. Ritchie. It contained 1 C— CH_3 (Found: 3.6%. Calc. for $C_{17}H_{26}O_{10}$: CH_3 , 3.8%).

(a) *Loganin 2,4-dinitrophenylhydrazone*.—Loganin (200 mg) was added in aqueous solution to 2,4-dinitrophenylhydrazine in 2N hydrochloric acid. The derivative slowly precipitated and was removed by filtration after 6 hr. It formed an orange powder, m.p. 262 °C, insoluble in most solvents, but recrystallized from a large volume of dioxan (Found: C, 47.4; H, 5.2; N, 10.6; OCH_3 , 5.0%. Calc. for $C_{22}H_{26}O_{12}N_4[OCH_3]$: C, 48.4; H, 5.3; N, 9.8; OCH_3 , 5.4%). It was too insoluble to carry out an ultraviolet absorption measurement.

(b) *Hydrogenation*.—Attempts failed to hydrogenate at atmospheric pressure loganin in aqueous ethanol or acetic acid with Adams's catalyst, or penta-acetyl-loganin with palladium-charcoal in ethyl acetate.

(c) *Reduction*.—(i) A Clemmensen reduction of loganin gave a small amount of volatile oil with a marked odour, soluble in conc. hydrochloric acid to a cherry-red solution; it may be a furan derivative. The non-volatile portion was a resin from which no pure compound could be isolated. Brief heating with hydriodic acid (d, 1.7) converted loganin into a black tar.

(ii) Loganin (3 g) in hot ethanol (20 c.c.) was added to liquid ammonia (100 c.c.) and reduced by the addition of sodium (1.5 g). Water (50 c.c.) was then added and the solution evaporated to dryness under reduced pressure. The product was then acetylated by heating with acetic anhydride (30 c.c.) for 2 hr, excess evaporated under reduced pressure, and water (15 c.c.) added to the residue. The precipitated oil slowly crystallized and was recrystallized from ethanol as needles, m.p. 126 °C, $[\alpha]_D^{25} -53^\circ$ (chloroform). It had no detectable absorption in the ultraviolet

between 230–350 $m\mu$ (Found: C, 54.6; H, 6.7; Ac, 40.4%. Calc. for $C_{28}H_{42}O_{15}[Ac_6]$: C, 54.4; H, 6.8; Ac, 41.7%).

(d) *Penta-acetyl-loganic Acid*.—Loganin (1 g) in water (10 c.c.) was heated on the steam-bath for 15 min with barium hydroxide (1 g). The solution was acidified to pH 3 with dil. sulphuric acid, the barium sulphate removed by filtration and the solution evaporated to dryness at 30 °C under reduced pressure. The residue was a deliquescent gum which could not be crystallized, but which was precipitated as a white powder, m.p. c. 250 °C by adding acetone to a concentrated aqueous solution. It was converted to *penta-acetyl-loganic acid* by the method used by Merz and Krebs (1937) for loganin. This was more soluble in aqueous acetic acid than *penta-acetyl-loganin* and was extracted with chloroform. It crystallized from methanol or ethanol and a little water as fluffy needles, m.p. 98 °C and m.p. 158 °C (Found: C, 53.8; H, 5.8%; OCH_3 , nil. Calc. for $C_{26}H_{34}O_{15}$: C, 53.2; H, 5.8%). It was soluble in sodium bicarbonate solution, and was reprecipitated unchanged by the addition of acid; it gave no colour with ferric chloride. Diazomethane in ether acting on a methanol solution gave *penta-acetyl-loganin*, m.p. 132 °C, $[\alpha]_D^{20}$ —80° (chloroform) undepressed by an authentic specimen, m.p. 132–134 °C, $[\alpha]_D^{20}$ —80° (chloroform).

In another experiment, the solution was slowly distilled during hydrolysis (2 c.c. distillate) and the distillate tested by the method of Denigès (1910) for methanol. A violet colour confirmed its presence.

(e) *Ozonolysis*.—*Penta-acetyl-loganin* (2 g) in ethyl acetate (20 c.c.) was ozonized (approx. 5% ozone in oxygen) at 0 °C for 4 hr, when ozone was emerging freely. To the solution was added acetic acid (3 c.c.), water (1 c.c.), and zinc dust (5 g) with shaking, the solution becoming warm. After filtration the solution was washed with small amounts of aqueous sodium bicarbonate and carbonate, neither of which extracted any appreciable amount of material other than acetic acid. The solution was dried (sodium sulphate) and evaporated under reduced pressure. To the residue was added methanol (4 c.c.) and water to incipient turbidity. After leaving in the refrigerator crystals slowly separated. Two different compounds were obtained in different experiments (c. 100 mg) and it is not clear at present what are the conditions for producing one or the other: A, m.p. 60 °C from methanol and B, m.p. 155 °C from methanol. After heating with acetic anhydride-sodium acetate the evaporated mother liquor from B gave *penta-acetyl- β -glucose*, m.p. 125–127 °C (Found: C, 49.2; H, 5.6%. Calc. for $C_{16}H_{22}O_{11}$: C, 49.3; H, 5.6%) undepressed by an authentic specimen, m.p. 127 °C. Compounds A and B may well be isomeric: A (Found: C, 50.95; H, 5.9; OCH_3 , 5.0%. Calc. for $C_{27}H_{34}O_{17}$: C, 51.1; H, 6.0; $1 \times OCH_3$, 4.85%); B (Found: C, 51.15; H, 6.2; OCH_3 , 5.0%). Neither compound showed any detectable selective absorption between 230–350 $m\mu$, and no ketonic or acidic properties could be detected.

Acetaldehyde (2,4-dinitrophenylhydrazone, m.p. 164 °C, undepressed by an authentic specimen) was easily recognized as being formed on the ozonolysis by distilling about 4 c.c. of the solvent into 2,4-dinitrophenylhydrazine in 2N hydrochloric acid and rapidly working up. A blank test with the solvent after treatment with ozone gave only a slight amount of resinous derivative by the same procedure.

VI. ACKNOWLEDGMENTS

The authors are indebted to Dr. G. K. Hughes and Dr. E. Ritchie for a gift of loganin, and to Mr. R. L. Werner for an infra-red absorption spectrum.

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β -TRIKETONES

III. XANTHOSTEMONE*

By A. J. BIRCH† and PATRICIA ELLIOTT‡

[Manuscript received December 16, 1955]

Summary

Xanthostemone, $C_{18}H_{16}O_3$, by its properties and by oxidation reactions is shown to have formula I.

I. INTRODUCTION

Steam distillation of the air-dried leaves of *Xanthostemon oppositifolius* Bail., a member of the family Myrtaceae, gave in 0.22 per cent. yield an oil which was almost completely soluble in sodium carbonate solution. On distillation a new substance, xanthostemone, $C_{18}H_{16}O_3$, was obtained. This closely resembled in its general properties dehydroangustione (II) (Birch and Elliott 1956). It gave a red ferric test, the ultraviolet absorption had maxima at λ 231 m μ , $\log \epsilon$ 4.03; λ 280 m μ , $\log \epsilon$ 3.82 (cf. dehydroangustione λ 230 m μ , $\log \epsilon$ 4.05; λ 282 m μ , $\log \epsilon$ 3.76). It contained no OMe and the Kuhn-Roth estimation indicated less than 1 C-Me. However, other members of this series (Birch and Elliott 1956) gave similar low values and it seems probable that 2 C-Me are present. The infra-red absorption curve showed a series of strong bands in the region of 6-7.5 μ as with other β -triketones (Birch 1951). It gave a 2,4-dinitrophenylhydrazone, $C_{18}H_{20}O_6N_4$, m.p. 239 °C.

Oxidation of xanthostemone with alkaline hypobromite gave rise to a lower fatty acid and an acid $C_7H_{10}O_4$, m.p. 132 °C, which is probably identical with 2,2-dimethylglutaconic acid (III), m.p. 134 °C (Perkin and Smith 1903), of which none was available for comparison. Hydrolysis with 50 per cent. sulphuric acid gave what is almost certainly isobutyric acid, recognized by paper chromatography, together with a colourless substance $C_8H_{10}O_2$, m.p. 150.5 °C, with the properties of a β -diketone, and which is to be formulated as IV. Its ultraviolet absorption at λ_{\max} 233 m μ , $\log \epsilon$ 4.04; λ_{\max} 280 m μ , $\log \epsilon$ 3.79 is similar to that of the trimethylcyclohexendione similarly produced from dehydroangustione. Confirmation of the presence of gem-dimethyl groups in the ring was provided by oxidizing xanthostemone with permanganate to obtain dimethylmalonic acid. Hydrogenation of xanthostemone, followed by hydrolysis, gave a β -diketone, $C_8H_{12}O_2$, m.p. 104 °C, indicating further the presence of a double

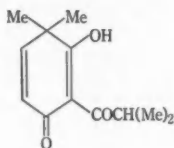
* Birch and Elliott (1955) may be regarded as Part II of this series.

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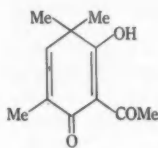
‡ Department of Organic Chemistry, University of Sydney.

bond in the ring. These data can be accommodated only on the basis of formula I for xanthostemone.

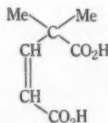
Xanthostemone is therefore a homologue of dehydroangustione (II), and its biosynthesis is presumably similar (cf. Birch and Elliott 1956). It is of interest that the initial acid is isobutyric rather than acetic acid, and that only two methyl groups are present in the ring. There can be no doubt in this case as to the position of the double bond, and its discovery adds further weight to the biosynthetic hypotheses already put forward (Birch, Elliott, and Penfold 1954; Birch and Elliott 1956).



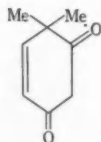
(I)



(II)



(III)



(IV)

II. EXPERIMENTAL

Air-dried leaves and terminal branchlets (20 lb) of *Xanthostemon oppositifolius*, "Southern Penda", obtained from Como, via Ku Ku, Queensland, were steam distilled for 9 hr. The distillate (40 gal) was extracted with ether to yield 20 c.c. of oil giving an intense red ferric test. The oil was extracted with aqueous sodium bicarbonate, carbonate, and hydroxide successively, the bulk being soluble in the carbonate solution. Acidification and distillation gave xanthostemone, b.p. 95–102 °C/0.8 mm (mainly at the higher temperature), $[\alpha]_D^{20}$ 0° (c, 2.37 in chloroform), n_D^{24} 1.5112 (Found: C, 70.1; H, 7.9; OMe, nil; C-Me, 5.6%. Calc. for $C_{12}H_{16}O_3$ (2C-Me): C, 69.2; H, 7.7; C-Me, 14.4%). It was recovered unchanged after refluxing for 2 hr with aqueous sodium hydroxide (10%). The 2,4-dinitrophenylhydrazone formed orange-red needles, m.p. 239 °C from a large volume of methanol (Found: C, 55.4; H, 5.4%. Calc. for $C_{18}H_{20}O_4N_4$: C, 55.7; H, 5.2%).

(a) *Oxidation of Xanthostemone.*—(i) *Hypobromite.* The substance (100 mg) in aqueous sodium hydroxide (4 c.c.; 10%) was reacted at room temperature for 1 hr with bromine (240 mg) in sodium hydroxide solution (10 c.c.; 10%). The bromoform was removed, excess hypobromite destroyed by the addition of sodium sulphite, and the solution acidified. Several extractions with ether, and extraction of the ether with sodium bicarbonate and acidification gave an acid, m.p. 132 °C from benzene-light petroleum (b.p. 60–90 °C) (Found: C, 53.0; H, 6.1%. Calc. for $C_7H_{10}O_4$: C, 53.2; H, 6.4%).

(ii) *Permanganate.* Xanthostemone (1 g) in acetone (40 c.c.) was treated with finely powdered potassium permanganate (1.2 g) in small portions with shaking. After 1 hr, water

(4 c.c.) was added and a further 2 g of potassium permanganate. After 3 hr, a further 1 g of permanganate was added and the mixture left overnight. The manganese dioxide was removed by filtration and washed with water (40 c.c.), the extract being added to the evaporated acetone solution. After filtration, the aqueous extract was evaporated under reduced pressure to 6 c.c. and acidified. Extraction with ether (10 × 10 c.c.) and evaporation gave dimethylmalonic acid recrystallized from benzene-light petroleum (b.p. 60–90 °C), m.p. 187 °C undepressed by an authentic specimen.

(b) *Hydrolysis of Xanthostemone*.—Xanthostemone (1 g) was heated on a steam-bath with aqueous sulphuric acid (4 c.c.; 50%). The mixture was diluted with water and extracted with ether, and the ether shaken with sodium bicarbonate solution to give (A) ether-soluble and (B) acidic fractions. Fraction A on evaporation of the ether gave a colourless solid, m.p. 105–5 °C, from benzene-light petroleum (b.p. 60–90 °C) which is apparently 4,4-dimethylcyclohexan-1,3-dione (Found: C, 69.1; H, 7.2%. Calc. for $C_8H_{10}O_2$: C, 69.5; H, 7.3%). Fraction B was acidified and steam distilled. The distillate, smelling strongly of lower fatty acid, was extracted with butanol and chromatographed on paper by the method of Lindqvist and Storgards (1953), the distances travelled being measured relative to acetic acid (R_A); possible acids were run for comparison. Several experiments gave consistent results; one is quoted: isobutyric acid, R_A 2.20; hydrolysis acid, R_A 2.20; isovaleric acid, R_A 3.00; n-butyric, R_A 2.30. The acid is therefore almost certainly isobutyric acid.

(c) *Hydrogenation of Xanthostemone*.—Xanthostemone (400 mg) in ethanol was hydrogenated with Adams's catalyst until hydrogen (44 c.c.; 1 mole) had been absorbed. After evaporation of the solvent the residual oil was hydrolysed as above with sulphuric acid (50%) to give colourless crystals, m.p. 104 °C, from benzene-light petroleum (b.p. 60–90 °C) presumably 4,4-dimethylcyclohexan-1,3-dione (Found: C, 68.2; H, 8.7%. Calc. for $C_8H_{12}O_2$: C, 68.5; H, 8.6%).

III. ACKNOWLEDGMENTS

We are greatly indebted to Mr. J. G. Tracey and Mr. L. J. Webb, C.S.I.R.O. Phytochemical Survey, for collection of the leaves, to Mr. A. R. Penfold and his staff for steam distillation of the oil, and to the Rockefeller Foundation (New York) for financial support.

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NATURAL DERIVATIVES OF FURAN

II. THE STRUCTURE OF EVODONE

By A. J. BIRCH* and R. W. RICKARDS†

[Manuscript received November 18, 1955]

Summary

2-Acetyl-5-methylcyclohexan-1,3-dione (IV) has been synthesized and is probably identical with a degradation product of evodone. On the basis of this synthesis and of published work, evodone is probably III.

I. INTRODUCTION

Evodone, $C_{10}H_{12}O_2$, $[\alpha]_D^{26} -53.9^\circ$, m.p. $73^\circ C$, was isolated from *Evodia hortensis* Forst. by van Hulssen (1941). The substance is an unsaturated ketone, λ_{max} 265 $m\mu$, $\log \epsilon_{max}$ 3.57, and on oxidation with permanganate gives methylsuccinic acid. Ozonolysis produces a compound, $C_9H_{12}O_3$ (according to published analyses; $C_9H_{10}O_3$ is erroneously given in several places), m.p. $42.5^\circ C$, which gives a ferric colour and has λ_{max} 270 $m\mu$, $\log \epsilon_{max}$ 3.94. Hydrogenation gives a mixture including a substance $C_{10}H_{16}O_2$, m.p. $160^\circ C$ which is still a ketone, and reduction under Clemmensen conditions and oxidation gives β -methyladipic acid. Among the products of ozonolysis is stated to be formaldehyde, but no indications of amount or method of detection are given. van Hulssen considered evodone to have formula I.

A more satisfactory formula appears to us to be III. Against I are several indications. The ozonolysis product II should have the formula $C_9H_{10}O_3$, instead of $C_9H_{12}O_3$ which analyses clearly indicate; there also seems no reason why II should give a ferric test. The ultraviolet absorption maximum of II would probably not be at longer wavelengths than 245 $m\mu$; the figure found is 270 $m\mu$. The 2,4-dinitrophenylhydrazone of evodone has m.p. $258-260^\circ C$, which is in the range found for aromatic ketones; from general experience the derivative of I would be expected to have a m.p. at least a hundred degrees lower than this.

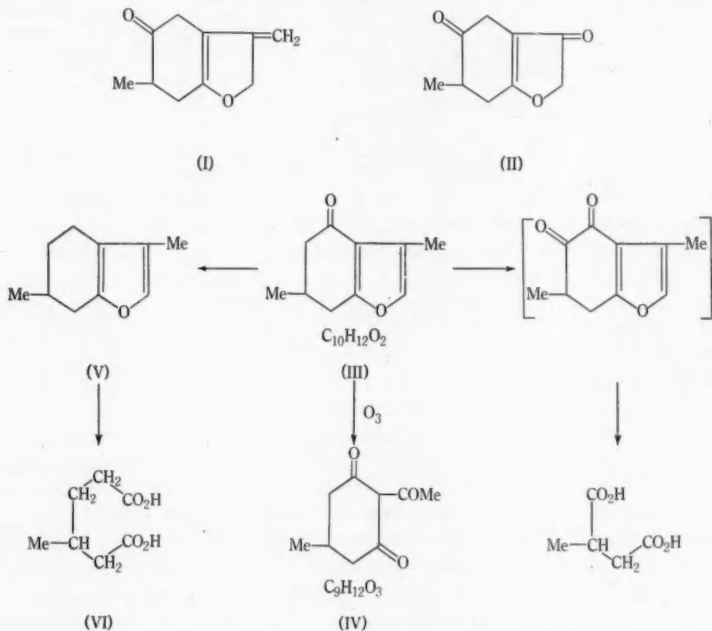
Structure III explains all the known reactions and properties of evodone, except the formation of formaldehyde on ozonolysis. In the absence of evidence as to the amount formed, this observation must be treated with reserve, since small amounts of formaldehyde frequently result from the ozonolysis of compounds not containing $C=CH_2$. The nearest analogue of III, of which the ultraviolet spectrum is recorded in the literature, is 2-acetylfuran, which has λ_{max} 266–267 $m\mu$ (Abe 1938) (cf. evodone λ_{max} 265 $m\mu$). 2-Acetyl-5,5-dimethylcyclohexan-1,3-dione has an absorption band at 277 $m\mu$, $\log \epsilon$ 4.0 (Birch and

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Todd 1952); the ozonolysis product now formulated as IV has λ_{\max} 270 $m\mu$, $\log \epsilon_{\max}$ 3.94. The product of Clemmensen reduction of III would be menthofuran (V) which is known to give β -methyladipic acid (VI) on oxidation (Wienhaus and Dewein 1934).

Clearly IV is the key-compound and its synthesis was undertaken by standard methods. Orcinol dimethyl ether was reduced with sodium and ethanol in liquid ammonia to the 2,5-dihydro-derivative (cf. Birch 1950), and acid hydrolysis gave 5-methylcyclohexan-1,3-dione. This was refluxed with acetic anhydride-sodium acetate to form 2-acetyl-5-methylcyclohexan-1,3-dione (IV), m.p. 42.5–44 °C with absorption maxima at 235 $m\mu$, $\log \epsilon$ 3.83 and 270 $m\mu$,



$\log \epsilon$ 4.11, giving the expected red ferric test. These properties agree with those found by van Hulssen for the ozonolysis product of evodone. He did not examine the ultraviolet spectrum in the region of 235 $m\mu$. We have so far been unable to obtain authentic evodone, but we are convinced on the above evidence that the formula is in fact III, and attempts to synthesize this substance are in progress. Evodone is therefore probably a ketomenthofuran, and another member of the series of natural furans related to terpenes.

II. EXPERIMENTAL

Orcinol dimethyl ether (7.4 g) in ethanol (20 c.c.) and liquid ammonia (100 c.c.) was reduced by adding sodium (5 g) in small pieces over 10 min with swirling. Water (75 c.c.) was added, the product taken up in ether, dried over potassium carbonate, the ether evaporated, and the

residue heated on the steam-bath for 10 min with N hydrochloric acid (5 c.c.). The product was taken up in ether (35 c.c.) and extracted with sodium hydroxide solution (5%). Acidification and extraction with ether gave 5-methylcyclohexan-1,3-dione (4.4 g) which crystallized on evaporation of the ether and was recrystallized from water, m.p. 127–128 °C (Found: C, 66.7; H, 8.0%. Calc. for $C_7H_{10}O_2$: C, 66.6; H, 8.0%). This substance (2.0 g), acetic anhydride, and anhydrous sodium acetate (3.0 g) were refluxed for 3 hr, the excess of anhydride decomposed with water, and the solution extracted with ether. After washing the extract with saturated bicarbonate solution, the product was extracted with aqueous sodium hydroxide (5%). Acidification and ether extraction gave an oil which solidified in ice, and was recrystallized twice from light petroleum (b.p. 60–90 °C) (ice-cooling) and then from aqueous ethanol. The 2-acetyl-5-methylcyclohexan-1,3-dione (0.90 g) formed colourless glistening plates, m.p. 42.5–44 °C (Found: C, 64.2; H, 7.2%. Calc. for $C_9H_{12}O_3$: C, 64.3; H, 7.2%).

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THE TAUTOMERISM OF 6-HYDROXY-4-METHYLDIHYDROFURO-(2',3',2,3)PYRIDINE

By E. RITCHIE*

[Manuscript received October 24, 1955]

Summary

The claim, that two tautomeric forms, of which 6-hydroxy-4-methyldihydrofuro-(2',3',2,3)pyridine is one, may be isolated, could not be substantiated.

I. INTRODUCTION

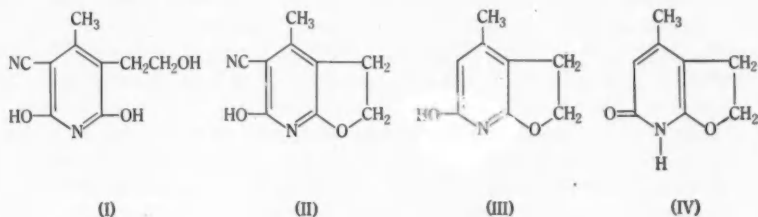
By the action of boiling concentrated hydrochloric acid on ethyl 4-cyano-3-methyl-6-phenoxy-2-hexenoate Matejka, Robinson, and Watt (1932) obtained 2,6-dihydroxy-4-methyl-3-phenoxyethylpyridine as the chief product, together with a smaller amount of a substance $C_8H_9O_2N$, m.p. 249–250 °C. It was insoluble in weak alkalis, gave a reddish purple ferric test, and was formulated by them as 6-hydroxy-4-methyldihydrofuro(2',3',2,3)pyridine (III).

The same substance was later prepared by Stevens, Beutel, and Chamberlin (1942) by a different series of reactions. They condensed ethyl cyanoacetate with acetylbutyrolactone and ammonia and isolated the ammonium salt of 5-cyano-2,6-dihydroxy-3-hydroxyethyl-4-methylpyridine (I), which on boiling for a short time with concentrated hydrochloric acid gave 5-cyano-6-hydroxy-4-methyldihydrofuro(2',3',2,3)pyridine (II). When either II or the ammonium salt of I was heated in a sealed tube at 150 °C for 8 hr with concentrated hydrochloric acid a mixture of two isomers was obtained. One of them, $C_8H_9O_2N$ had m.p. 250 °C, was sparingly soluble in ethyl acetate, gave a strong ferric test, and was identical with the substance obtained by Matejka, Robinson, and Watt (1932). The other, m.p. 177–5–179 °C, which formed 10–30 per cent. of the total yield, was very soluble in ethyl acetate, and gave a negative ferric test. The ultraviolet absorption spectra of the isomers differed markedly, III having λ_{max} . 295 m μ , $\log \epsilon_{max}$. 3.69 and λ_{max} . 326 m μ , $\log \epsilon_{max}$. 3.44, and its isomer λ_{max} . 247 m μ (broad), $\log \epsilon_{max}$. 3.89.† It was claimed that either substance could be converted to an equilibrium mixture by heating with concentrated hydrochloric acid at 150 °C for 4 hr, or by dissolving in 10 per cent. alkali, and allowing to stand for a short time at room temperature. Also each substance gave 3-(2'-chloroethyl)-2,6-dichloro-4-methylpyridine by heating with phosphorus oxychloride at 180 °C. It was therefore concluded that the substances were tautomers, the isomer of higher m.p. being the hydroxypyridine form III and the isomer of lower m.p. the pyridone form IV.

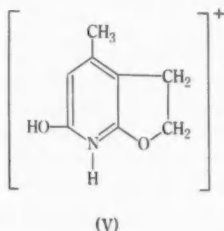
* Department of Organic Chemistry, University of Sydney.

† These values were read from graphs.

This claim is of some importance since this instance appeared to be the only well-authenticated case of an actual isolation of amide-imidol tautomers (Elderfield 1950), but the evidence for it was not completely convincing. In particular it was difficult to understand why it was necessary to heat with concentrated hydrochloric acid at 150 °C for 4 hr to obtain equilibration. It would have been expected, that mere dissolution in mineral acid would have converted either form into the same cation V and that more vigorous treatment with acid would have had no effect. From the cation, III would be regenerated by loss of a



proton from the nitrogen and IV by loss of a proton from the oxygen. On the other hand, since the isomers would be only very weakly acidic, it was conceivable that it was necessary to use the alkaline conditions described to obtain equilibration. Again, the ultraviolet absorption spectra of the alleged tautomers were not related in the manner which would have been expected on the basis of the work of Specker and Gawrosch (1942), who examined the spectra of 2-pyridone and its *O*- and *N*-alkyl derivatives. The whole matter was therefore re-examined.



The initial condensation of ammonia, ethyl cyanoacetate, and acetylbutyrolactone was first described by Guareschi (1905), but his work was evidently overlooked, possibly because he stated that he used "hydroxyethyl acetoacetic ester" and because the structure of his product was printed incorrectly. However, there can be no doubt that he did obtain the substance I. On re-examination, it was found that the yields of the ammonium salt of I claimed by Stevens, Beutel, and Chamberlin (1942) could be duplicated provided the reaction time was considerably extended. The condensation could also be effected by substituting cyanoacetamide for ethyl cyanoacetate in which case piperidine could be used as the catalyst and the ammonia omitted, but there was little to

be gained in the use of these variants. On the addition of hydrochloric acid to a cold aqueous solution of the ammonium salt the free dihydroxypyridine (I) was precipitated, but short boiling of I, or its ammonium salt with concentrated hydrochloric acid resulted in cyclization to II. The cyano-group remained unchanged probably because of the very slight solubility of II which separated from the boiling reaction mixture. However, it could be removed by heating with concentrated hydrochloric acid at 150 °C for 8 hr, the conditions used by Stevens, Beutel, and Chamberlin (*loc. cit.*), but the product occasionally contained appreciable amounts of II. A more convenient method was to reflux for 10 hr with concentrated hydrobromic acid, the procedure adopted in a similar case by Ruzicka and Fornasir (1919). The product from these reactions was isolated by three different methods, but the same result was obtained in each case. The product $C_5H_6O_2N$ formed in about 75 per cent. yield, had m.p. 245–247 °C and behaved as a single substance contaminated with only traces of impurities. After recrystallization it had m.p. 250 °C, gave a reddish purple ferric test, and was identical with the substance III of Stevens, Beutel, and Chamberlin. It will be referred to below as the dihydrofuropyridine. All attempts to isolate from the crude material a second substance were fruitless.

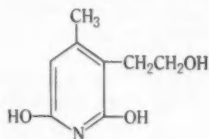
The original filtrates from which the product had been precipitated and which were nearly neutral, gradually turned deep blue on standing at room temperature and more rapidly on heating. This behaviour is shown by many derivatives of 2,6-dihydroxypyridine (e.g. Ruzicka and Fornasir 1919), but on working up the filtrates the only isolable products were traces of the dihydrofuropyridine and small amounts of another substance which could not be purified.

After the failures to isolate the second tautomeric form in these experiments attention was turned to the conversion of the dihydrofuropyridine to the equilibrium mixture. A solution of the dihydrofuropyridine in excess 10 per cent. sodium hydroxide was kept at room temperature for 24 hr and then neutralized with acetic acid at 0 °C. The pure starting material was recovered quantitatively and the same result was obtained when its solution in 10 per cent. sodium hydroxide was refluxed for 3 hr. In these experiments the filtrates from the precipitation of the product did not become blue on standing, and there can be no doubt that the dihydrofuropyridine was completely unaltered.

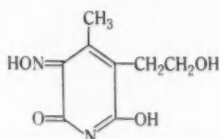
The action of acid was then studied. After the substance had been heated with concentrated acid at 150 °C for 4 hr it could be recovered in about 75 per cent. yield, as in its preparation, and again no second substance could be isolated but the filtrates became blue on exposure to air. Refluxing with concentrated hydrobromic acid also gave the same result.

The approximately constant recovery of the dihydrofuropyridine and the presumed formation of a 2,6-dihydroxypyridine suggested that the dihydrofuran ring was reversibly opened by acid and the failure to isolate the 2,6-dihydroxypyridine could be attributed to its unfavourable solubilities and ready oxidation by air. Support for this hypothesis was readily obtained. The dihydrofuropyridine was unaffected by short treatment (10 min) with N hydrochloric acid at room temperature but on refluxing it gave a substance, $C_5H_{11}O_3N$, in 58 per

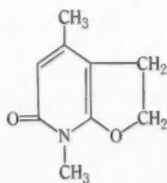
cent. yield after 1 hr and 63 per cent. yield after 4 hr, with 34 and 30 per cent. recovery of starting material respectively. The substance was easily soluble in hot water and ethanol and crystallized out on cooling only if fairly pure. It was sparingly soluble in other organic solvents but dissolved in aqueous sodium carbonate with effervescence. Its neutral aqueous solution gradually became blue on exposure to air but if warmed with ammonia it rapidly became very deep blue. It gave a violet-red ferric test which quickly faded because of reduction of the ferric to ferrous iron. Ammoniacal silver nitrate was immediately reduced and silver nitrate itself on standing. These properties are characteristic of 2,6-dihydroxypyridines (Ruhemann 1893; Rogerson and Thorpe 1905; Gibson and Simonsen 1929) and final proof that it was 2,6-dihydroxy-3-hydroxyethyl-4-methyl pyridine (VI) was obtained by its reaction



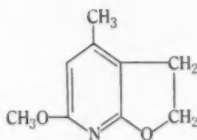
(VI)



(VII)



(VIII)



(IX)

with nitrous acid to form an isonitroso-derivative (VII), which gave a deep red solution with aqueous sodium carbonate or ammonia and a green colour with aqueous ferrous sulphate. When VI was refluxed with N hydrochloric acid for 4 hr, 65 per cent. was recovered and the dihydrofuropyridine was isolated in 32 per cent. yield. The reversibility of the hydrolysis of the dihydrofuran ring under acid conditions was therefore established. However, when VI was refluxed with concentrated hydrobromic acid the dihydrofuropyridine was obtained in 85 per cent. yield, but none of the starting material could be isolated although the neutralized filtrate became blue on keeping. The failure to recover VI from this and similar reactions described above was probably due to the prevention of its crystallization by impurities, arising from decomposition or further reaction with the concentrated acid at the comparatively high temperatures. It may be concluded, however, that hydrolysis of the dihydrofuran

ring is favoured by dilute acid and ring closure by concentrated acid and that treatment with acid does not partially isomerize the dihydrofuropyridine.

The dihydrofuropyridine could not be acetylated with acetic anhydride in the presence of pyridine at 100 °C. With dimethyl sulphate in alkaline solution it afforded 1,4-dimethyldihydrofuro(2',3',2,3)-6-pyridone (VIII) as the sole isolable product. This substance was also the chief product of the reaction with diazomethane but from the mother liquors a small amount of the isomeric *O*-methyl derivative (IX) was isolated as its picrate. On regeneration it was obtained as a colourless gum.

Ultraviolet absorption data for the substances III, VIII, and IX are illustrated in Figure 1. The λ_{\max} values (235, 295, 326 m μ) found for III are in good agreement with those read from the curve for the hydroxypyridine tautomer,

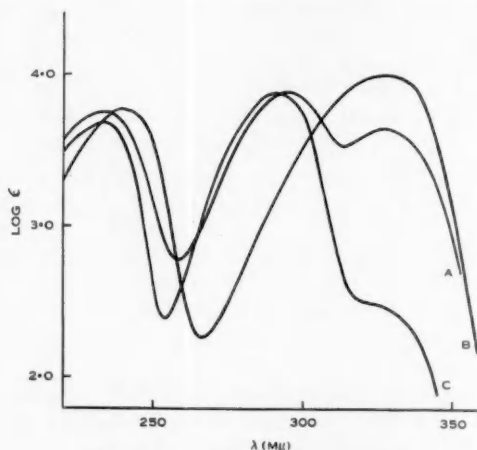


Fig. 1.—Ultraviolet absorption spectra.

- (a) Substance III.
- (b) Substance VIII.
- (c) Substance IX.

given by Stevens, Beutel, and Chamberlin (*loc. cit.*) but the intensities ($\log \epsilon_{\max}$, 3.74, 3.87, 3.62 respectively) are rather higher. Specker and Gawrosch (1942) found that the spectrum of 2-pyridone was almost identical with that of *N*-methyl-2-pyridone but was quite different from that of 2-ethoxypyridine which absorbed at shorter wavelengths. From this evidence it may be concluded that in neutral solution the substance exists primarily in the 2-pyridone form. In the present case, the characteristic bands of both the *N*-methyl derivative (VIII) (λ_{\max} , 326 m μ , $\log \epsilon_{\max}$, 3.98) and the *O*-methyl derivative (IX) (λ_{\max} , 290 m μ , $\log \epsilon_{\max}$, 3.86) are evident in the curve for III. However, the curve for IX corresponds more closely to the curve for III than does that for VIII, from which it follows that in the tautomeric equilibrium existing in III the hydroxypyridine form predominates.

II. EXPERIMENTAL

Melting points are uncorrected. Analyses are due to Dr. G. Weiler and ultraviolet absorption data to Dr. F. B. Strauss and Mr. F. Hastings, Dyson Perrins Laboratory, Oxford.

(a) *5-Cyano-2,6-dihydroxy-3-hydroxyethyl-4-methylpyridine*.—(i) To acetylbutyrolactone (12.8 g; 0.1 mol.) and ethyl cyanoacetate (11.3 g; 0.1 mol.) was gradually added concentrated ammonia (30 ml) with shaking. The mixture became warm and a voluminous white solid separated which dissolved on continued shaking. After keeping at room temperature for 2 weeks the ammonium salt which had commenced to separate after 1 day, was collected, washed thoroughly with ethanol, and dried at room temperature (13.6 g, 65% yield). For analysis it was purified by dissolving a portion (1 g) in hot water (10 ml) adding boiling absolute ethanol (200 ml), filtering, and allowing to cool. Repetition of the process gave small colourless needles which began to darken at about 250 °C and effervesced at about 290 °C (Found: C, 51.3; H, 6.1; N, 19.6%. Calc. for $C_9H_{13}O_3N_2$: C, 51.2; H, 6.2; N, 19.9%). On short boiling its aqueous solution became slightly purple. It gave a blue-violet ferric test.

The salt (5 g) was dissolved in hot water (50 ml), the solution quickly cooled and made just acid to Congo red with 3N hydrochloric acid. A crystalline precipitate soon began to form and after thorough cooling in an ice-bath it was collected and washed with a little ice-water. Recrystallization from water gave colourless plates (3.8 g, 80%), which became yellow at about 200 °C and effervesced at about 315 °C (Found: C, 55.6; H, 5.2%. Calc. for $C_9H_{10}O_3N_2$: C, 55.7; H, 5.2%). It gave a blue-violet ferric test.

(ii) A mixture of cyanoacetamide (4.2 g; 0.05 mol.), acetylbutyrolactone (6.4 g; 0.05 mol.), and concentrated ammonia (15 ml) was shaken until all solids had dissolved and then kept at room temperature for 8 days. The ammonium salt (7.3 g, 70%) was collected, washed with ethanol, and dried.

(iii) A solution of acetylbutyrolactone (6.4 g), cyanoacetamide (4.2 g), and piperidine (4.5 g) in ethanol (25 ml) was kept at 40 °C for 3 days and then evaporated on the water-bath. The dark residue was dissolved in water, the solution filtered, acidified, and cooled in an ice-bath. Recrystallization of the precipitate from water with the aid of charcoal gave the product (4.8 g, 50%).

(b) *5-Cyano-6-hydroxy-4-methyl-dihydrofuro(2',3',2,3)pyridine*.—The above dihydroxy-pyridine (3 g), or its ammonium salt, and concentrated hydrochloric acid (30 ml) was heated under reflux. The solid rapidly dissolved but after 15 min a precipitate began to form. After a further 15 min the mixture was cooled, diluted, and the product (90% yield) collected. It crystallized from a large volume of methanol in colourless prismatic needles which became yellow at about 250 °C and then darkened rapidly as the temperature was raised (Found: C, 61.3; H, 4.7%. Calc. for $C_9H_9O_2N_2$: C, 61.4; H, 4.6%). It gave a weak greenish brown ferric test in methanol.

(c) *6-Hydroxy-4-methyldihydrofuro(2',3',2,3)pyridine*.—Either I, its ammonium salt, or II, could be used, but usually I was chosen since it was most readily purified.

(i) A mixture of I (5 g) and concentrated hydrochloric acid (25 ml) was heated in a sealed tube at 250 °C for 8 hr. After cooling, the tube was opened, warmed, and the contents filtered from any II that was present. The filtrate was worked up by either of the following methods.

(1) Water (50 ml) was added, the solution cooled in ice, made slightly alkaline with ammonia, and then neutralized with acetic acid. After several hours at 0 °C the product (2.9 g, 75%), m.p. 245–247 °C, after sintering at about 235 °C, was collected and washed thoroughly with water. From the filtrate which became blue on standing, further small amounts (about 0.01–0.05 g) of crude product could be isolated by evaporation to a small volume and keeping. Further evaporation occasionally gave dark brown gummy material (0.1 g) which could not be purified.

(2) The filtrate was evaporated to dryness under reduced pressure on the water-bath, the residue dissolved in hot water (50 ml), and a hot concentrated solution of sodium acetate (14 g) added. The precipitate was collected, washed, and dried. The results were as above.

(3) The filtrate was evaporated to dryness under reduced pressure on the water-bath, the residue dissolved in hot water (50 ml), the solution cooled and treated with 10% sodium hydroxide until the precipitate first formed just redissolved. The solution was then acidified with acetic acid and the product collected after cooling at 0 °C. The results were as above.

(ii) The cyano compound I (32 g) was refluxed with concentrated hydrobromic acid (320 ml) for 10 hr. After cooling, the solution was divided into three equal portions which were worked up by the three above methods. The results were the same.

Extraction of the crude product with boiling ethyl acetate or fractional crystallization from methanol failed to reveal the presence of more than one substance. The pure substance crystallized in small colourless prisms, m.p. 250 °C (Found: C, 63.6; H, 6.0; N, 9.4%. Calc. for $C_6H_6O_2N$: C, 63.6; H, 5.9; N, 9.3%). It was soluble in boiling 3% potassium carbonate and in hot 3N acetic acid. From the latter solvent it crystallized unchanged in curved plant-like forms. It gave a purplish red ferric test. The substance was recovered quantitatively after boiling with 10% sodium hydroxide for 3 hr or treating with acetic anhydride and pyridine at 100 °C for 1 hr.

The *picrate* crystallized from ethanol in small pale yellow needles, m.p. 195–196 °C (decomp.) (Found: C, 44.5; H, 3.5%. Calc. for $C_{14}H_{12}O_6N_4$: C, 44.2; H, 3.2%).

(d) *Action of Concentrated Acid.*—The substance (10 g) was heated in a sealed tube with concentrated hydrochloric acid (40 ml) at 150 °C for 4 hr or refluxed with concentrated hydrobromic acid (100 ml) for 4 hr. By working up either of the reaction mixtures by either of the three procedures given in Section II (c), 75–80% of the starting material, m.p. 246–248 °C could be recovered. The other results were also the same.

(e) *Action of N Hydrochloric Acid.*—(i) A solution of the substance (8 g) in N hydrochloric acid (100 ml) was refluxed for 1 hr and then treated with a hot concentrated solution of sodium acetate (20 g). The precipitate which formed immediately was filtered from the hot liquid, washed, and dried. The product (2.7 g, 34%), m.p. 248–250 °C after darkening slightly at about 245 °C was unchanged starting material. The filtrate was rapidly boiled down to about 25 ml and cooled in ice. The crystalline material (5.3 g, 58%) was collected, washed with a little ice-water, and dried.

(ii) The above experiment was repeated except that refluxing was continued for 4 hr. Starting material (2.4 g, 30%), m.p. 248–250 °C, and hydrolysed product (5.7 g, 63%) were recovered.

2,6-Dihydroxy-3-hydroxyethyl-4-methylpyridine crystallized from ethanol in small colourless prismatic needles, m.p. 160 °C (Found: C, 56.6; H, 6.9; N, 8.0%. Calc. for $C_8H_{11}O_3N$: C, 56.8; H, 6.6; N, 8.3%). It was sparingly soluble in non-hydroxylic organic solvents and dissolved readily in hot water separating on cooling in a hydrated form, m.p. 144–146 °C with effervescence.

(f) *Action of Acid on VI.*—(i) The substance (4 g) was refluxed with N hydrochloric acid (50 ml) for 4 hr and the products isolated as in Section II (e). The dihydrofuropyridine (1.1 g, 32%), m.p. 248–250 °C, and the substance VI (2.6 g, 65%) were recovered.

(ii) The substance (4 g) was refluxed with concentrated hydrobromic acid (50 ml) for 4 hr. After removing excess acid under reduced pressure on the water-bath the products were isolated as in Section II (e). Only the dihydrofuropyridine (3.0 g, 85%), m.p. 248–250 °C could be obtained.

(g) *Nitrosation of VI.*—A solution of sodium nitrite (0.6 g; 1.5 mol.) in water (2 ml) was added in one lot to a solution of VI (1 g) in water (20 ml) and acetic acid (2 ml) at 25 °C. The mixture became slightly warm and in a few minutes a yellow crystalline precipitate began to form. After 10 min the mixture was cooled in ice, the product collected, washed, dried, and recrystallized from ethyl acetate. It formed yellow prisms which became greenish at about 150 °C, then darker and finally went black, and effervesced at 190–194 °C (Found: C, 48.5, H, 5.2%. Calc. for $C_8H_{10}O_4N_2$: C, 48.5; H, 5.1%). It was readily soluble in hot water and hot ethanol. It dissolved in dilute ammonia or sodium carbonate to give deep red solutions. Its aqueous solution gave a green colour with ferrous sulphate.

(h) *Methylation of III.*—(i) To a solution of the substance (1.5 g) and sodium hydroxide (1 g) in water (15 ml) methyl sulphate (1.5 ml) was added and the mixture shaken until the oily drops disappeared. More sodium hydroxide (1 g), water (15 ml), and methyl sulphate (1.5 ml) were added and the mixture shaken. After repeating the process again, the clear solution was extracted with chloroform (5 × 40 ml), the extract dried, and evaporated. The crystalline residue after several recrystallizations from light petroleum (b.p. 60–80 °C) afforded colourless needles (0.9 g), m.p. 121–122 °C, b.p. 195–197 °C/15 mm, of the *N*-methyl derivative (Found: C, 64.7; H, 6.8%. Calc. for $C_9H_{11}O_2N$: C, 65.4; H, 6.8%). It was easily soluble in water and the usual organic solvents. It was very hygroscopic and short exposure to the air lowered the m.p. to 80–90 °C. It gave a red ferric test. The substance was unaffected by hot concentrated hydrochloric acid and could not be acetylated by acetic anhydride-sulphuric acid at 100 °C.

The *picrate* crystallized from ethanol in yellow needles which sintered at 168 °C and decomposed at 172–173 °C (Found: C, 45.7; H, 3.9; OCH_3 , nil; NCH_3 , 4.4%. Calc. for $C_{18}H_{14}O_6N_4$: C, 45.7; H, 3.6; $1 \times NCH_3$, 7.4%).

(ii) The substance (3 g) was stirred with methanol (25 ml) at 0 °C and treated with ethereal diazomethane (100 ml from 10 g nitrosomethylurea). After about 2 hr a clear solution was obtained, which was kept overnight, and then evaporated. The residue on recrystallization from light petroleum (b.p. 60–80 °C) (150 ml) gave the *N*-methyl derivative (2.0 g), m.p. and mixed m.p. 119 °C. The filtrate was concentrated to about 20 ml and kept. The liquid was decanted from a second crop of crude *N*-methyl derivative (0.5 g) and evaporated to dryness. The residue was treated with ethanolic picric acid and the mixed *picrates* dissolved in boiling ethyl acetate. On standing the *picrate* of the *N*-methyl derivative (0.1 g), m.p. and mixed m.p. 169–170 °C separated. The filtrate was evaporated and the residue repeatedly recrystallized from a little ethanol, giving, finally, the *picrate* of the *O*-methyl derivative (0.2 g) as clumps of yellow needles, m.p. 113–114 °C (Found: C, 45.6; H, 3.7; OCH_3 , 7.5%. Calc. for $C_{15}H_{14}O_6N_4$: C, 45.7; H, 3.6; $1 \times OCH_3$, 7.9%).

III. ACKNOWLEDGMENTS

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C¹⁴-INTRAMOLECULAR ISOTOPE EFFECTS OF MALONIC AND BROMOMALONIC ACIDS

By E. C. M. GRIGG*

[Manuscript received December 8, 1955]

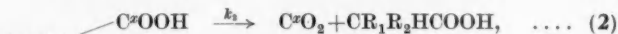
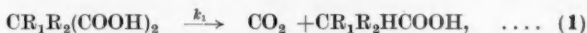
Summary

The C¹⁴-intramolecular isotope effects for the decarboxylations of malonic and bromomalonic acids have been determined at the m.p.'s of the acids. In addition, the C¹⁴-intramolecular isotope effect for malonic acid in quinoline solution has been measured between 85 and 135 °C.

I. INTRODUCTION

A number of papers have been published on the C¹⁴-intramolecular isotope effects of malonic acid at its melting point. However, the agreement between these sets of results is not good, and in most cases the consistency within any one given set is poor. No papers have been published on C¹⁴ isotope solvent effect. For bromomalonic acid, two papers have appeared with widely varying values. In every case the experimental values are much higher than that calculated from the theoretical treatment (Bigeleisen 1949, 1951) based on the absolute reaction rate theory.

The rate constants for the decarboxylation of malonic acids may be written :



where x is 13 or 14.

The ratio k_3/k_2 which determines the relative rates of rupture of C¹³-C¹³ and C¹³-C^x bonds is given by

$$\frac{k_3}{k_2} = \left(\frac{m_2^*}{m_3^*} \right)^{\frac{1}{2}}, \quad \dots (4)$$

where the m^* 's are the effective masses of the activated complexes along the coordinates of decomposition, and are calculated as being the reduced mass across the bond being broken. This gives a value for k_3/k_2 of 1.038 for C¹⁴-labelling. This ratio is invariant with temperature.

Table 1 summarizes the average values of intramolecular isotope effects expressed as $100[(k_3/k_2) - 1]$.

The oxidation of the malonic acids and acetic acid reported in these papers has been carried out either by a wet combustion technique such as the Van

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Slyke-Folch method or by oxidation over CuO at 700–800 °C. In most cases, the decarboxylation products have been removed by an inert gas sweep. In the present paper, a batch technique was used, followed by vacuum distillations to separate the products.

TABLE I

C¹⁴-INTRAMOLECULAR ISOTOPE EFFECTS FOR MALONIC ACID (MA) AND BROMOMALONIC ACID (BrMA)

Acid	Isotope Effect (%)	References
MA	12.0	Yankwich and Calvin (1949)
MA	6.0	Roe and Hellman (1951)
MA	10.3	Yankwich, Stivers, and Nystrom (1952)
MA	9.9	Yankwich and Stivers (1953)
MA	5.45	Yankwich, Promislow, and Nystrom (1954)
Theoretical MA ..	3.8	
BrMA	41.0	Yankwich and Calvin (1949)
BrMA	11.6	Yankwich and Stivers (1953)
Theoretical BrMA ..	3.8	

II. EXPERIMENTAL

(a) Materials

C¹⁴-labelled sodium cyanide was prepared (Jeanes 1953) by heating C¹⁴-labelled barium carbonate, zinc dust, and metallic sodium in a stream of ammonia at 650 °C. The product was acidified with dilute 2N sulphuric acid and distilled into sodium hydroxide solution.

Malonic acid-1-C¹⁴ was prepared (Yankwich and Stivers 1953) from the labelled cyanide by reaction with chloroacetic acid followed by hydrolysis of the resulting cyanoacetic acid. The product was recrystallized three times from a 1:1 by volume mixture of acetone and benzene and, finally, sublimed twice *in vacuo* (Found: C, 34.6; H, 3.9%. Calc. for C₃H₄O₄: C, 34.6; H, 3.9%).

Bromomalonic acid-1-C¹⁴ was prepared by slowly adding bromine to malonic acid-1-C¹⁴ as described by Yankwich and Stivers (1953). The product was recrystallized three times and evacuated, at room temperature, for 5 days. Finally, it was evacuated for 7 hr at 60 °C (Found: C 19.6; H, 1.8%. Calc. for C₃H₃O₄Br: C, 19.7; H, 1.7%).

Carbonate-free sodium hydroxide was prepared (Clark 1923) by the electrolysis of a saturated solution of analytical reagent sodium chloride. Quinoline was purified by fractional distillation under reduced pressure.

(b) Procedure

Glass reaction bulbs, containing two side arms, one of which had a breakable seal, were prepared. A weighed sample of malonic or bromomalonic acid was placed in a small bulb which was then connected to a vacuum system and evacuated. The bulb was sealed off and heated in a furnace for 16 hr. For the decarboxylations of the solid acids, the furnace was kept at 140 °C for

malonic acid and 118 °C for bromomalonic acid. After the bulb had cooled to room temperature it was sealed again to the vacuum system, and the bulb cooled in a dry ice-acetone bath to condense the acetic acid. The seal was broken and the carbon dioxide was distilled out into a U tube cooled with liquid air. Any traces of acetic acid were removed from the carbon dioxide by three sublimations between dry ice and liquid air temperatures. Finally, the carbon dioxide was frozen in liquid air and pumped at 10^{-5} mm Hg for an hour. The acetic acid was vacuum transferred to a tap vessel, which was then attached to a combustion train. The combustion tube had a Pregl-filling of CuO, Ag, and PbO₂. The acids were decomposed at 750 °C. The carbon dioxide formed was passed through three dry ice traps. Finally, it was sublimed three times from a dry ice to a liquid air trap, then frozen in liquid air, and pumped at 10^{-5} mm Hg for an hour. A similar technique was used when a solvent was used. The solvent was removed by vacuum distillations.

Isotopic assays were carried out on the carbon dioxide both as a gas and as solid barium carbonate by a Geiger-Müller counting assembly. In the case of solid counting the carbon dioxide was frozen into carbonate-free sodium hydroxide solution, and the barium carbonate precipitated with excess ammoniacal barium chloride solution. The barium carbonate was mounted and counted by an end-window Geiger counter (window 1.7 mg/cm²). The gas fractions were subdivided into 15 or more samples for individual counting. This subdivision was carried out by volume measurements in a gas burette. The solid barium carbonate samples weighed 6.58 ± 0.07 mg. An activity balance was made to make sure that no activity was lost. The usual corrections for radioactive assays were applied. The activities were checked against a substandard. Coincidence corrections were made using multiple paired-source measurements. Each count was sufficiently long to reduce the standard deviation to less than 0.5 per cent. Each count was checked at least 10 times.

III. RESULTS

The decomposition of malonic acid has been shown to be first order. Radioactive analysis of the carbon dioxide gives a value for its specific activity which is proportional to $(C^{14}O_2)/[(C^{14}O_2) + (C^{12}O_2)]$, where n is the normal mixture of stable isotopes. Using the rate constants defined by equations (1), (2), and (3), it can be shown that:

$$\frac{(C^{14}O_2)}{[(C^{14}O_2) + (CO_2)]} = \frac{M^{14}(1 - e^{-(k_2 - k_3)t})k_2}{M(1 - e^{-k_1t}) + M^{14}(1 - e^{-(k_2 + k_3)t})(k_2 + k_3)}, \quad \dots (5)$$

where M and M^{14} are the initial number of moles of ordinary and of labelled malonic acids.

Therefore, at $t = \infty$,

$$\frac{(C^{14}O_2)}{[(C^{14}O_2) + (CO_2)]} = \frac{M^{14}}{M + M^{14}} \cdot \frac{k_2}{k_2 + k_3},$$

therefore

$$\frac{k_2}{k_3} = \left[\frac{M^{14}/(M + M^{14})}{(C^{14}O_2)/(C^{14}O_2 + CO_2)} \right] - 1, \quad \dots (6)$$

and

$$\frac{k_3}{k_2} = \frac{A^{14}/(A+A^{14})}{M^{14}/(M+M^{14}) - A^{14}/(A+A^{14})}, \quad \dots \quad (7)$$

where $A = (\text{CR}_1\text{R}_2\text{HCOOH})$ and $A^{14} = (\text{CR}_1\text{R}_2\text{HC}^{14}\text{OOH})$.

The values

$$\frac{(\text{C}^{14}\text{O}_2)}{[(\text{C}^{14}\text{O}_2) + (\text{CO}_2)]}, \quad \frac{M^{14}}{M+M^{14}}, \quad \text{and} \quad \frac{A^{14}}{A+A^{14}}$$

are the molar specific activities, S_c , S_M , and S_A respectively. Hence, equations (6) and (7) may be rewritten as

$$\frac{k_3}{k_2} = \frac{S_M}{S_c} - 1, \quad \dots \quad (8)$$

and

$$\frac{k_3}{k_2} = \frac{S_A}{S_M - S_A}. \quad \dots \quad (9)$$

By combining equations (8) and (9) we obtain

$$\frac{k_3}{k_2} = \frac{S_A}{S_c}. \quad \dots \quad (10)$$

The molar specific activities of the effluent carbon dioxide, the monoacid, and the diacid are listed in Table 2. Each value is a mean of at least 15 samples.

TABLE 2
MEAN SPECIFIC ACTIVITIES OF MALONIC ACID, BROMOMALONIC ACID, AND THEIR
DECARBOXYLATION PRODUCTS

Run No.	Mean Values of Specific Activities ($\mu\text{c}/\text{mM}$)		
	S_c	S_A	S_M
Malonic acid (temp. 140 °C)			
1	0.0882	0.0931	0.1813
2	0.0881	0.0931	0.1813
3	0.0880	0.0930	0.1812
4	0.0879	0.0932	0.1811
5	0.0880	0.0931	0.1810
6	0.0880	0.0933	0.1813
7	0.0882	0.0932	0.1815
Bromomalonic acid (temp. 118 °C)			
1	0.0879	0.0934	0.1813
2	0.0877	0.0935	0.1814
3	0.0876	0.0932	0.1810
4	0.0875	0.0934	0.1811
5	0.0878	0.0933	0.1812
6	0.0876	0.0934	0.1811
7	0.0878	0.0934	0.1812

Each of these samples was counted 10 times to standard deviation of at least 0.5 per cent. These specific activities are the average values obtained from the individual counts on the subdivided carbon dioxide samples.

The percentage isotope effects $100[(k_3/k_2)-1]$ are listed in Table 3. These values have been calculated from equations (8), (9), and (10).

The agreement between the calculations by the three different equations gives a measure of the internal consistency of the data. However, only two of the three values are independent and, therefore, the average values are calculated from equations (8) and (9) only. The average value for malonic acid is 5.77 with a standard deviation of 0.20, and for bromomalonic 6.46 with a standard deviation of 0.24. These results are still much higher than the theoretical value of 3.8, but are lower than those obtained by most other workers. There is a

TABLE 3
C¹⁴-INTRAMOLECULAR ISOTOPE EFFECTS FOR MALONIC AND BROMOMALONIC ACIDS

Run No.	Percentage Isotope Effect $100[(k_3/k_2)-1]$		
	From Eqn. (8)	Eqn. (9)	Eqn. (10)
Malonic acid (140 °C)			
1	5.56	5.56	5.56
2	5.79	5.56	5.68
3	5.90	5.45	5.69
4	6.03	6.03	6.03
5	5.69	5.92	5.80
6	6.02	6.02	6.02
7	5.78	5.55	5.67
Bromomalonic acid (118 °C)			
1	6.26	6.26	6.26
2	6.84	6.37	6.61
3	6.63	6.15	6.39
4	6.97	6.50	6.74
5	6.38	6.15	6.27
6	6.74	6.50	6.62
7	6.38	6.38	6.38

possibility in the above technique of a change in the activity of CO₂ by exchange reactions or during the purification process. Experiments were carried out to test this possibility by mixing C¹⁴O₂ and CH₃COOH; the normal experimental procedure was carried out, but no appreciable exchange was found. The disagreement among the results from various workers is difficult to explain. It was found, in this laboratory, that when the decarboxylation products were removed by an inert gas sweep, the results were much more variable, than when a batch technique such as described above was used. When wet oxidation procedures have been used, any isotope effect due to the monoacid can be ignored provided these oxidations were quantitative.

Table 4 presents the C¹⁴ isotope effects for the decarboxylation of the acid in quinoline solution. There is an increase in the isotope effect with temperature

decrease. Yankwich and Belford (1954) found a similar effect for the C¹³ isotope effects. Theory predicts a value of 1.98 for the C¹³ isotope effect and 3.8 for the C¹⁴ isotope effect, at any temperature. It appears that in quinoline solution additional isotope effects are impressed on the intramolecular isotope effect. This solvent isotope effect could be due to reversible equilibria between malonic acid and the solvent.

TABLE 4

C¹⁴-INTRAMOLECULAR ISOTOPE EFFECTS FOR MALONIC ACID IN QUINOLINE

Temp. (°C)	135	125	115	105	95	85
Average 100 [(k ₃ /k ₂) - 1]	6.0	6.5	7.0	7.5	8.1	8.5

Investigations are proceeding into C¹⁴ isotope effects of malonic acid and substituted malonic acids at their melting points and in various solvents.

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THE ALKALOIDS OF *SENECIO JACOBAEA* L.

II. THE STRUCTURES OF THE ACIDS, AND THE RELATIONSHIP BETWEEN JACOBINE AND JACONINE

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Summary

A study has been made of the "necic" acids formed by hydrolysis from the pyrrolizidine bases of *Senecio jacobaea* L., in particular jaconecic acid and its derivatives, and certain tentative conclusions have been reached concerning the structure of these compounds. Jacobine and jaconine are interconvertible by addition and loss of hydrogen chloride, which is accompanied by reversal in sign of optical rotation. It is suggested that jacobine contains an ethylene oxide ring and jaconine is the corresponding chlorohydrin. Jacoline on alkaline hydrolysis yields retronecine and an oily acid which forms a solid dilactone acetate. Jacozine has been hydrolysed to jacozinecic acid which appears to be new.

I. INTRODUCTION

The isolation of five alkaloids from *Senecio jacobaea* L. has previously been reported from these laboratories (Bradbury and Culvenor 1954a, 1954b), and a short account of the relationship between jacobine and jaconine and of the structure of jaconecic acid has appeared (Bradbury 1954). The infra-red spectrum of jacobine in 0.01M carbon tetrachloride solution shows a band at 3525 cm^{-1} , due to the presence of a free hydroxyl group. This frequency is abnormally low, the general range for absorption by this group being $3590\text{--}3650\text{ cm}^{-1}$. The molar extinction (about 72) is of the right order of magnitude for one hydroxyl group (Marion, Ramsay, and Jones 1951). The band, greatly broadened by association, is shown by the solid at about 3165 cm^{-1} . Either of the bands at 1035 and 1068 cm^{-1} can be attributed to the deformation frequency of a primary hydroxyl group (Zeiss and Tsutsui 1953). The doubling of the carbonyl frequency, even in solution (1734 and 1749 cm^{-1}), indicates two ester groups having different environments. There is no sign of absorption in the $1640\text{--}1660\text{ cm}^{-1}$ region, but this does not necessarily preclude the existence of an isolated double bond in a molecule of such high molecular weight. The

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
existence of bands at 838, 907, and 1258 cm^{-1} is consistent with the presence of an ethylene oxide ring.*

Jaconine and its hydrochloride have previously (Bradbury and Culvenor 1954b) been assigned the formulae $\text{C}_{20}\text{H}_{32}\text{O}_7\text{NCl}$ and $\text{C}_{20}\text{H}_{33}\text{O}_7\text{NCl}_2$ respectively, and were provisionally regarded as containing one molecule of ethanol of crystallization (Bradbury 1954). Because of the low ethanol content previously reported for jacoline (2.6%; calc. 10.4%), the matter has been reinvestigated. This alkaloid retains methanol and ethanol as solvent of crystallization but alkoxyl analyses do not agree with a stoichiometric formula, the highest ethoxyl value being 5.2 per cent. Similarly jacoline hydrochloride gave an ethoxyl figure of 8.1 per cent. (calc. 9.6%). Complete removal of these solvents is not achieved by drying at 100°C under vacuum. However, when jacoline is crystallized from carbon tetrachloride and dried under vacuum at 100°C a product analysing in agreement with the formula $\text{C}_{18}\text{H}_{26}\text{O}_6\text{NCl}$ is obtained.

Solvent-free jacoline in the solid state shows bands at 3480 and 3620 cm^{-1} . The latter band provides some evidence for the presence of a tertiary hydroxyl group (Sears and Kitchen 1949; Smith and Creitz 1951). In solution in carbon tetrachloride there is a strong band at 3525 cm^{-1} , which has a molar extinction coefficient of the right order of magnitude for two hydroxyl groups. As in jacobine, the carbonyl frequency is doubled and the presence of two different ester groups confirmed. Absorption in the double bond region is absent.

The alkaloids jacobine and jacoline on alkaline hydrolysis yield retronecine and a mixture of two isomeric acids of the formula $\text{C}_{10}\text{H}_{16}\text{O}_6$ - jaconecic acid, m.p. 181°C, $[\alpha]_D +29^\circ$, and isojaconecic acid, m.p. 113–114°C, $[\alpha]_D +75^\circ$. Of these only the former has previously been obtained. Hydrolysis of these alkaloids with 15 per cent. hydrochloric acid according to the procedure of Zhdanovich and Men'shikov (1941) yields a compound $\text{C}_{10}\text{H}_{13}\text{O}_4\text{Cl}$ which has the same properties as, and is probably identical with the compound obtained by these workers from othosenine. The chlorine must be covalently bound in the acid part of the molecule, for hydrolysis of jacoline with hydrobromic acid affords

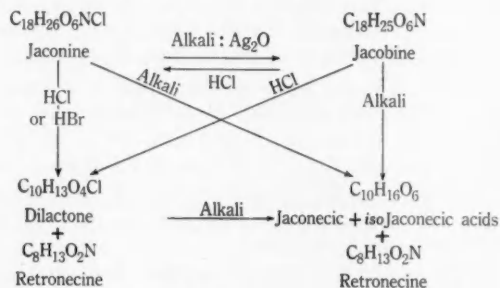
* Field, Cole, and Woodford (1950), from a study of a limited number of fairly simple ethylene oxides, concluded that though these compounds all show bands near 1250, 1165, and 865 cm^{-1} , which are close to characteristic frequencies of the ethylene oxide molecule, only the band at 1250 cm^{-1} can be identified with reasonable certainty as being due to the ethylene oxide group.

It may be pointed out here that the 1165 cm^{-1} frequency cannot be characteristic of the 

group as such, because it arises from a C-H deformation mode and will not occur if the carbon atoms are fully substituted (Herzberg 1945; Stone 1954). Shreve *et al.* (1951) studied solutions of the epoxides of a number of long-chain alcohols, acids, and esters and concluded that characteristic bands are found near 1250 cm^{-1} and at 882–917 cm^{-1} (*trans*-epoxy) and 829–838 cm^{-1} (*cis*-epoxy). Patterson (1954) gave wider limits for the frequency ranges of the bands near 900 and 830 cm^{-1} .

Unfortunately, most compounds absorb in the 800–900 cm^{-1} region, and many oxygen-containing substances such as acids and esters absorb near 1250 cm^{-1} , so that the above correlations can at the best be used in a negative way only, that is, absence of bands near 1250, 900, and 830 cm^{-1} may be taken to indicate absence of an ethylene oxide group, but the presence of bands near any or all of these frequencies does not prove the presence of this group.

the same chloro-compound. It yields jaconecic and *isojaconecic* acids on alkaline hydrolysis. Jacobine and jaconine are therefore closely related, differing only by a molecule of hydrogen chloride, and this is readily added or withdrawn with interconversion of jacobine and jaconine. When jacobine is neutralized with one mol. hydrochloric acid, jacobine hydrochloride, which like the free base is laevorotatory, is obtained. With two mol. hydrochloric acid dextrorotatory jaconine hydrochloride is obtained, and the free base of the same sign of rotation, still containing one atom of chlorine, can be obtained by treatment with a slight excess of ammonia. Jaconine reverts to jacobine in the presence of either excess aqueous sodium hydroxide or silver oxide in water. The relationship therefore exists:



Jaconecic acid is readily isolated from the alkaline hydrolysis of jacobine, jaconine, or the compound $\text{C}_{10}\text{H}_{13}\text{O}_4\text{Cl}$ by ether extraction of the acidified hydrolysate and recrystallization of the residue from ethyl acetate. However, the yield is far from quantitative, and the mother liquors from hydrolysis of jacobine or jaconine always yield a considerable amount of non-crystalline material which has a higher rotation than jaconecic acid. Paper chromatography using butanol saturated with 5 per cent. aqueous acetic acid as the mobile phase and bromocresol green for printing shows the presence of three components of R_F 0.93, 0.76, and 0.51. These can be separated by partition chromatography on silica gel, and are found to be the monoethyl ester of jaconecic acid, *isojaconecic* acid, and jaconecic acid respectively (see Table 3). The monoethyl ester of jaconecic acid can be hydrolysed to jaconecic acid, and is undoubtedly formed by *trans*-esterification with the ethyl acetate used for recrystallization.

Jaconecic acid contains three carbon methyl groups, is dibasic, and yields a liquid dimethyl ester and a solid dibasic monoacetate. It gives a faint reaction with ferric chloride, and oxidation with lead tetra-acetate gives one mol. carbon dioxide. It consumes only 0.23 mol. periodic acid under conditions (Jackson 1944) which normally split α -glycols (Table 3), and therefore cannot contain two adjacent hydroxyl groups. It is recovered unchanged on refluxing with 15 per cent. hydrochloric acid. Jaconecic acid fails to hydrogenate over platinum and shows no absorption in the infra-red or ultraviolet characteristic of isolated or conjugated double bonds. The presence of an alcoholic hydroxyl group cannot be checked by measurements of the 3600 cm^{-1} region, owing to the very

low solubility of the acid in both chloroform and carbon tetrachloride, but the presence of a strong band in the "Nujol" mull at 1069 cm^{-1} is consistent with the presence of a primary hydroxyl group. The bands at 1690 and 1735 cm^{-1} (solid) or 1717 and 1749 cm^{-1} (chloroform solution) can be attributed to carboxylic acid groups, one without and one with an electron-attracting substituent.* When the carboxylic acid groups in jaconecic acid are esterified, that having an electron-attracting α -substituent is the first to be attacked, as the lower frequency band persists in the monoester but disappears in the diester. Dimethyl jaconecate in the liquid state shows a shoulder at 3300 cm^{-1} and a band at 3550 cm^{-1} due to a free hydroxyl group. Esterification of the hydroxyl group in jaconecic acid leaves the carboxyl frequencies at much the same values, but introduces an ester group having a frequency (1758 cm^{-1}) considerably higher than that of ordinary acetates.

Absorption at 848 , 904 , and 1264 cm^{-1} in jaconecic acid is consistent with the presence of an epoxide ring, but in the mono- and diesters the presence of the ring is not strongly supported by the infra-red spectra.

Dimethyl jaconecate when reduced with lithium aluminium hydride gives an oil which reacts both with periodic acid (1 mole) (Table 3) and with lead tetra-acetate liberating formaldehyde. The presence of primary hydroxyl groups is indicated by bands at 3380 and 1059 cm^{-1} , and a double bond by absorption at 1647 cm^{-1} . The reduction product forms a tri-*p*-nitrobenzoyl derivative, m.p. 164°C , and a liquid triacetate, and analyses of both these derivatives indicate a formula $\text{C}_{10}\text{H}_{20}\text{O}_4$. There is thus a non-reactive oxygen, and possibly a double bond in the molecule. The infra-red spectrum of the triacetate shows adsorption at 3650 cm^{-1} in the liquid state, and this suggests the presence of a tertiary hydroxyl group (Sears and Kitchen 1949; Smith and Creitz 1951). A double bond is indicated by the band at 1644 cm^{-1} . On the other hand the tri-*p*-nitrobenzoyl derivative in the solid state, or in CCl_4 or CHCl_3 solution, shows almost complete lack of absorption in the region 3100 – 3650 cm^{-1} except for a very weak band at about 3470 cm^{-1} , which is certainly the first overtone of the ester carbonyl band. Absorption in the 1640 – 1680 cm^{-1} region is also absent, but this may be due to the high molecular weight of the compound. The absorption at 1609 cm^{-1} is due to the benzene rings. It is apparent that the crude reduction product contains an α -glycol group which is not present in jaconecic acid, and this clearly establishes the presence of an oxygen bearing substituent on the carbon atom α - to one carboxyl group. The double bond is apparently formed by dehydration of a penta-hydroxy intermediate formed by reduction and subsequent opening of an oxygen-containing ring.

* Electron-attracting substituents on the α -carbon atom of a carboxylic acid in general raise the frequency of the carbonyl vibration: thus acetic acid absorbs near 1720 cm^{-1} while chloroacetic acid, for instance, absorbs at 1735 cm^{-1} . Lactic acid absorbs at 1725 cm^{-1} (Flett 1951), but no systematic study has been made of the effect of α -substituents other than halogens. During the present investigation methoxyacetic, glycollic, and hydroxymalonic acid were measured both in the liquid state and in solution in carbon tetrachloride and in chloroform, and in each case the carbonyl absorption frequency lay close to 1740 cm^{-1} . An epoxide ring attached to the α -carbon atom should also raise the frequency.

*iso*Jaconecic acid, m.p. 113–114 °C, is also a dibasic acid. It is much more soluble in chloroform than jaconecic acid, and on acetylation with acetyl chloride does not yield a crystalline derivative, so that a primary hydroxyl group is probably absent. Virtual failure to react with periodic acid (Table 3) shows that an α -glycol group is not present. *iso*Jaconecic acid has only one carbonyl band at 1730 cm^{-1} in the solid state, but in chloroform solution there are two (1718 and 1773 cm^{-1}) and possibly also a shoulder at 1750 cm^{-1} . It shows no absorption in the infra-red or ultraviolet due to a double bond or conjugated double bonds.

The compound $\text{C}_{10}\text{H}_{13}\text{O}_4\text{Cl}$, m.p. 113 °C, $[\alpha]_{\text{D}} -26^\circ$, is neutral, contains no active hydrogen, and behaves as a lactone on titration. Attempts to replace the chlorine atom without rupture of the lactone rings have been unsuccessful. This compound shows no absorption in the 3100–3700 cm^{-1} region and hence contains no hydroxyl or carboxyl groups. Its carbonyl absorption, which occurs at 1781 cm^{-1} in chloroform solution, is split into two bands at 1770 and 1793 cm^{-1} in the solid state. Since there is no carbonyl absorption at lower frequencies it must be concluded that the two lactone rings are five-membered (Rasmussen and Brattain 1949). Alkaline hydrolysis of the dilactone and recovery of the products from the acidified solution show the presence of three compounds, which have been detected and separated by paper chromatography and partition chromatography on silica gel. Two of these have been identified as jaconecic and *iso*jaconecic acids respectively, while the third, an oil having an R_f of 0.79, $[\alpha]_{\text{D}} -10^\circ$, analysed according to the formula $\text{C}_{10}\text{H}_{14}\text{O}_5$. It is monobasic, contains a lactone ring, and the formula requires the presence of a double bond or an oxygen-containing ring. It has been designated as jaconecic monolactone. Neither jaconecic nor *iso*jaconecic acids can be reconverted to the dilactone $\text{C}_{10}\text{H}_{13}\text{O}_4\text{Cl}$ by refluxing with 15 per cent. hydrochloric acid.

Jaconecic monolactone shows a carbonyl frequency of 1753 cm^{-1} which is scarcely altered by dissolution. This frequency is a little high for a δ -lactone, and about 20 cm^{-1} too low for a γ -lactone (Rasmussen and Brattain 1949; Grove and Willis 1951). Absorption in this region could be due to an unsaturated γ -lactone (Ames, Bowman, and Grey 1954), but there is no sign of a double bond in the infra-red nor of a conjugated system in the ultraviolet spectrum. Although there is no indication of absorption by a carboxyl group its presence is indicated by titration. A band occurs at 1071 cm^{-1} , which is not far from the range 1075–1100 cm^{-1} quoted by Barrow and Searles (1953) as characteristic of a tetrahydrofuran ring.

The alkaloid jacoline (Bradbury and Culvenor loc. cit.) like jacobine and jaconine shows a double carbonyl frequency. It may contain a tertiary hydroxyl group (suggested by the absorption at 3500 cm^{-1} , which is scarcely altered by dissolution). On alkaline hydrolysis jacoline gives retronecine and an oily mixture of acids, from which no crystalline material can be obtained. However, on acetylation of the mixture with acetyl chloride a crystalline compound $\text{C}_{12}\text{H}_{16}\text{O}_6$, $[\alpha]_{\text{D}} +16.5^\circ$, jacolinecic dilactone acetate, can readily be obtained. This compound shows absorption at 1749 and 1781 cm^{-1} in solution (1745 and 1773 cm^{-1} in the solid), which indicates the presence of a γ -lactone and an ester

group. There is no hydroxyl absorption. Hydrolysis of jacolinecic dilactone acetate with alkali gives a crystalline monolactonic monobasic acid, m.p. 47 °C, $[\alpha]_D -21.7^\circ$, and having an R_F of 0.83. The analyses agree with a formula $C_{10}H_{14}O_5$. Absorption in the infra-red at 1773 and 1788 cm^{-1} in chloroform solution shows that it contains a γ -lactone ring. The absorption at 3550 cm^{-1} in the liquid state suggests that it may contain a tertiary hydroxyl group. Insufficient material was available for a thorough investigation of these compounds, but they are evidently closely related to those obtained from jacobine and jaconine. It is possible that jacoline and jaconine are the glycol and chlorohydrin respectively of the epoxide jacobine.

TABLE I
ULTRAVIOLET ABSORPTION SPECTRA

Substance	$\lambda_{\text{max.}}$ (m μ)	$\epsilon_{\text{max.}}$
Seneciphyllie acid*	217	5460
" " † (Adams and van Duuren 1953b) ..	214	8450
	214	8130
Jaconecic acid*	211	270
isoJaconecic acid*	215	242
Jaconecic monolactone*	222	276
Jacozinecic acid*	211	1138
Jacozine†	223	1731
Senecic acid*‡	219	4340
" " (Leisegang 1950)*	218.5	4950
" " (Kropman and Warren 1950)*	215	4100
" " (Adams and van Duuren 1953b)† ..	215	6195
Senecic (integerrinecic) acid lactone*‡	228	10270
" (Adams and van Duuren 1953a)	222	12000

* Solvent; water.

† Solvent, 95% ethanol.

‡ Specimens kindly provided by Mr. L. Smith of these laboratories.

The infra-red spectrum of jacozine (Bradbury and Culvenor loc. cit.) shows that it may contain a tertiary hydroxyl group, but unlike the other alkaloids it has only a single carbonyl frequency in the solid state, though the band is broadened on the low frequency side, and in solution is split into three. A band at 1647 cm^{-1} indicates the presence of a double bond. Alkaline hydrolysis of jacozine yields retronecine and jacozinecic acid, $C_{10}H_{14}O_6$, m.p. 161 °C, $[\alpha]_D -29.7^\circ$, which is a dibasic acid having two carbon methyl groups. The formula indicates double unsaturation, and both jacozine and jacozinecic acid show more pronounced absorption in the ultraviolet than does jaconecic acid (Table 1). A band at 1619 cm^{-1} in the infra-red is probably due to a conjugated double bond (Blout, Fields, and Karplus 1948), and carbonyl absorption occurs at 1688 and 1734 cm^{-1} in the solid state though only the second band appears in

solution. It may be that jacozinecic acid is an α -hydroxy acid, and that the 1688 cm^{-1} shoulder in the solid state is due to intermolecular interaction. Lactic acid, for instance, shows a shoulder at 1656 cm^{-1} which disappears in solution.

Acetylation of jacozinecic acid with acetyl chloride yields a compound $\text{C}_{12}\text{H}_{14}\text{O}_6$, m.p. 136 $^{\circ}\text{C}$, which contains one acetyl group. The infra-red spectrum

TABLE 2
INFRA-RED ABSORPTION FREQUENCIES (1600–1800 cm^{-1})

No.	Substance	Carbon Tetrachloride Solution (cm^{-1})	Chloroform Solution (cm^{-1})	Solid or Liquid (cm^{-1})
1	Jacobine	*	1724 (sh), 1734, 1749	1743, 1749
2	Jaconine	*	1728, 1741	1724, 1745
3	Jaconecic acid	*	1690 (?), 1717, 1749	1690, 1735
4	Acetyljaconecic acid	1735 (br)†	1747 (br)	1708, 1732, 1758
5	Monoethyl jaconecate	*	1720, 1741	1720, 1741
6	Dimethyl jaconecate	1741	1739	1741
7	Tetrahydroxy reduction product	*	*	1647
8	Triacetate of 7	*	*	1644, 1745
9	Tri- <i>p</i> -nitrobenzoate of 7	1735‡	1609, 1730	1609, 1732
10	Jaconecic dilactone	*	1781	1770, 1793
11	Jaconecic monolactone	*	1751	1753
12	isoJaconecic acid	*	1718, 1750 (?), 1773	1730
13	Jacoline	*	1722, 1732	1728, 1739
14	Jacolinecic monolactone	1775, 1792	1773, 1788	1773, 1786(ah)
15	Jacolinecic dilactone acetate ..	*	1749, 1781	1745, 1773
16	Jacozine	*	1722, 1735, 1751	1647, 1749(br)
17	Jacozinecic acid	*	1741	1619, 1688, 1734
18	Acetyljacozinecic anhydride ..	1755, 1786, 1825	1745, 1784, 1824	1745, 1779, 1820

* Not measured.

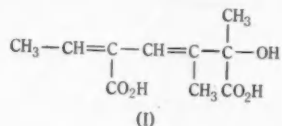
† br, broad; sh, shoulder.

‡ The 1600–1620 cm^{-1} region was obscured by solvent absorption.

shows bands typical of an ester and an anhydride, and an hydroxyl group is apparently still present. It has been tentatively called acetyljacozinecic anhydride.

Jacodine (Bradbury and Culvenor loc. cit.), previously identified as seneciophylline, has been hydrolysed to retronecine and an acid, m.p. 121–122 $^{\circ}\text{C}$, $[\alpha]_D -13.2^{\circ}$, having two carbon methyl groups. Adams and Govindachari (1948, 1949), Adams *et al.* (1952), and Adams and Hauserman (1952) report a

lower m.p. 114–115 °C for α -longinecic acid, and their carbon methyl determination, which agrees with ours, cannot be reconciled with their proposed formula :



The intensity and wavelength of absorption in the ultraviolet differ somewhat from the values reported by Adams and van Duuren (1953*a*, 1953*b*) for this compound (Table 1), but when it is considered that a compound of structure I can exist in eight different optically active forms, differences in ultraviolet spectra and melting point are to be expected. Comparison of the values obtained for senecic acid and its lactone by different investigators, and by using different solvents, also shows that there is considerable variation.

TABLE 3

R_F VALUES OF THE ACIDS AND THEIR REACTION WITH PERIODIC ACID

Substance	R_F Value	Mol. HIO_4 Consumed per Mol. Substance
Jaconecic acid	0.52	0.23
Acetyljaconecic acid	0.62	—
Monoethyl jaconecate	0.92	0.18
Tetrahydroxy reduction product, $\text{C}_{10}\text{H}_{20}\text{O}_4$	—	0.90
Jaconecic monolactone	0.79	0.44
isoJaconecic acid	0.76	0.10
Jacolinecic monolactone	0.83	—
Jacozinecic acid	0.42	0.17
Senecic acid	0.90	—
Seneciphylllic acid	0.87	0.71
Retronecic acid lactone	0.67	—
Heliotric acid	0.93	0.37
Trachelanthic acid	0.83	2.0
Lasiocarpic acid	0.80	2.0

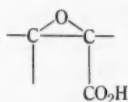
II. DISCUSSION

In attempting to deduce structural formulae for the acid moiety of the pyrrolizidine alkaloids, it does not necessarily follow that all structural features in the free acid obtained by hydrolysis must be present in the acid when it is esterified by retronecine. In the present work this fact is clearly demonstrated by the isolation of two isomeric acids from the alkaline hydrolysis of either jacobine or jaconine, and by the non-reactivity of either acid separately with

hydrogen chloride although such a reaction occurs when the acid is combined in the alkaloid. Any proposed structures must be consistent with the following :

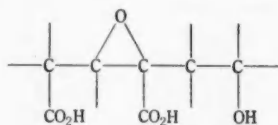
- (1) The presence of an epoxide group in jacobine and a chlorohydrin structure in jaconine.
- (2) Jaconecic acid contains an oxygen-containing substituent α - to one carboxyl group.
- (3) The dilactone $C_{10}H_{13}O_4Cl$ contains two γ -lactone rings.
- (4) Jaconecic acid contains three carbon methyl groups.
- (5) Jacobine and jaconecic acid contain a primary hydroxyl group.

It is thus probable that jaconecic acid as it occurs in jacobine contains the structure :



(II)

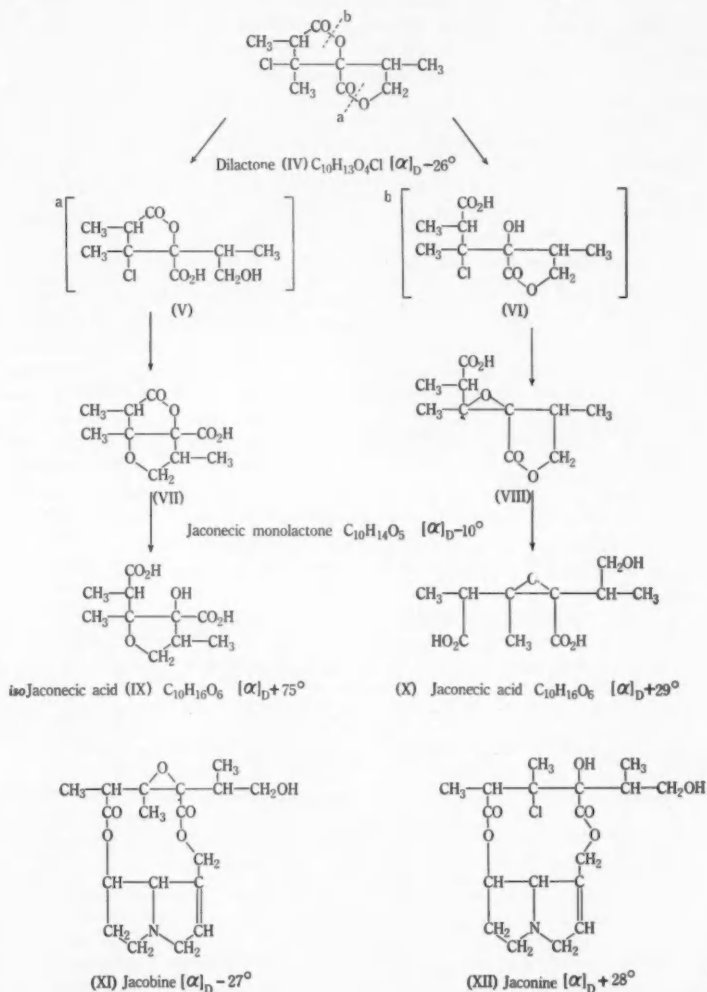
In order to form two five-membered lactone rings in the dilactone $C_{10}H_{13}O_4Cl$, the primary hydroxyl group of jaconecic acid must be placed on a carbon atom γ - to the carboxyl group, and the second carboxyl group γ - to one of the epoxide carbon atoms. Since glycidic acids generally react with halogen acids to give the β -halo-hydroxy acids, the second carboxyl group should be γ - to the α -carbon atom. Since the hydroxyl and second carboxyl group cannot be attached to the same carbon atom, and the hydroxyl group cannot be adjacent to the epoxide group, the expanded structure is :



(III)

At least four methods of joining two five-membered lactone rings together have previously been proposed (Bradbury 1954), but when the above limitations are imposed only one structure IV is feasible for the dilactone. Hydrolysis of the dilactone may occur at two positions *a* and *b*, and since there are two isomeric dibasic acids as products which are formed in almost equal quantities, it is apparent that the reactions are competitive. Two intermediates V and VI are possible, but because of the rapid elimination of hydrogen chloride under alkaline conditions have not been isolated. Jaconecic monolactone (VII or VIII) is sufficiently stable to be isolated in small yield, and its isolation indicates that the two lactone rings are hydrolysed at different rates, and that these reactions are also competitive with the elimination of hydrogen chloride. *iso*Jaconecic and jaconecic acids have been provisionally assigned formulae IX and X respectively. The lack of reactivity and the absence of decarboxylation of

jaconecic and *isojaconecic* acids with hydrochloric acid is difficult to reconcile with either of the free acids having structure X. However, jacobine and jaconine can best be represented by XI and XII or by the isomeric structures in which



esterification between the two hydroxyl and two carboxyl groups has taken place in the alternative manner. The reactions of these compounds are reminiscent of those occurring in the tropane series (Holmes 1950), in which

scopine, thought to contain an epoxide group, is an intermediate in the hydrolysis of *l*-scopolamine to scopine, to which either a tetrahydrofuran or a propylene oxide structure has been assigned.

III. EXPERIMENTAL

All melting points are corrected. Microanalyses were carried out in the C.S.I.R.O. Micro-analytical Laboratory.

Seneciphylllic Acid: Seneciphylline (20.8 g), hydrated barium hydroxide (40 g), and water (200 ml) were kept at 100 °C for 2 hr. The excess barium hydroxide was removed as barium carbonate, the filtrate acidified to Congo red with hydrochloric acid and continuously extracted with ether for 5 hr. Removal of the ether gave a viscous oil (11.3 g), which gave large colourless prisms from ether-light petroleum (b.p. 40–60 °C). When recrystallized from ethyl acetate it had m.p. 121–122 °C, $[\alpha]_D^{25} -13.7^\circ$ (c, 1.02 in water) (Found: C, 56.3; H, 6.9; CH_3C , 13.8 (1.5 hr oxidation) 13.5 (6 hr oxidation); equiv. (by titration), 110. Calc. for $\text{C}_{16}\text{H}_{14}\text{O}_5$: C, 56.1; H, 6.6; $2 \times \text{CH}_3\text{C}$, 14.0%; equiv., 107.1). Adams and Govindachari (1948, 1949) report m.p. 114–115 °C and $[\alpha]_D^{28} -13.25^\circ$ for α -longinecic acid.

(a) *Interconversion of Jacobine and Jaconine*.—(i) *Conversion of Jaconine Hydrochloride to Jacobine*. Jaconine hydrochloride of $[\alpha]_D^{25} +9.4^\circ$ (c, 1.27 in water) (4.68 g) dissolved in water (10 ml) was added dropwise to sodium hydroxide (1.6 g) in water (20 ml) with shaking. The chloroform extract after drying over sodium sulphate gave jacobine (3.3 g), $[\alpha]_D^{25} -20.9^\circ$ (c, 1.92 in chloroform). Repeated recrystallization from ethanol gave large colourless plates, m.p. 229–230 °C, $[\alpha]_D^{20} -29^\circ$ (c, 3.01 in chloroform). The specific rotations of -40 and -57° previously reported by us (Bradbury and Culvenor 1954a, 1954b) could not be repeated, and it is apparent that during isolation and purification of this base loss of optical activity occurs.

(ii) *Conversion of Jaconine Hydrochloride to Jaconine*. Jaconine hydrochloride (4.68 g) in water (10 ml) was added dropwise to dilute ammonia (50 ml), prepared from 0.880 ammonia (5 ml) and water (100 ml). The chloroform extract was washed with water, dried (Na_2SO_4) and distilled. The residue (3.95 g) gave colourless prisms, m.p. 146–147 °C, $[\alpha]_D^{17} +28.6^\circ$ (c, 1.54 in chloroform), $[\alpha]_D^{19} +29.7^\circ$ (c, 2.76 in ethanol).

(iii) *Conversion of Jaconine to Jacobine*. Jaconine of $[\alpha]_D^{17} +28.6^\circ$ (1.17 g), silver oxide (1.32 g), and distilled water (10 ml) were shaken together intermittently for 19 hr, and heated on a boiling water-bath for 3 hr. The silver chloride was filtered, thoroughly washed with chloroform, and the filtrate extracted with chloroform. The dried chloroform extracts yielded a slightly yellow solid (0.87 g), m.p. 222–223 °C, $[\alpha]_D^{16} -22.4^\circ$ (c, 2.14 in chloroform). Crystallization from ethanol gave large colourless plates, m.p. 229–230 °C, $[\alpha]_D^{27.7} -27.7^\circ$ (c, 2.95 in chloroform), undepressed on admixture with authentic jacobine.

(iv) *Preparation of Jacobine Hydrochloride*. Jacobine (1.0 g) dissolved in hot ethanol was treated with exactly 1 equiv. of 0.1N hydrochloric acid, and the solution was evaporated to dryness *in vacuo*. When recrystallized from ethanol colourless needles (0.71 g), m.p. 218 °C, $[\alpha]_D^{18} -10.9^\circ$ (c, 4.21 in water), which by further recrystallization was raised to m.p. 220 °C, $[\alpha]_D^{19} -14.7^\circ$ (c, 3.88 in water) (Found: N, 3.4; Cl, 9.4%. Calc. for $\text{C}_{15}\text{H}_{22}\text{O}_6\text{NCl}$: N, 3.6; Cl, 9.1%).

(v) *Conversion of Jacobine to Jaconine*. Jacobine (1.0 g) was dissolved in hot ethanol, and treated with 2 equiv. of 0.1N hydrochloric acid. The solution was evaporated to dryness, and the dry residue (1.24 g) was recrystallized from ethanol to give colourless needles, m.p. 204–205 °C (with effervescence), $[\alpha]_D^{17} +12.4^\circ$ (c, 3.86 in water). Treatment of this hydrochloride with ammonia as before gave jaconine $[\alpha]_D^{23} +27^\circ$ (c, 2.24 in chloroform). The high specific rotation previously reported by us (Bradbury and Culvenor loc. cit.) could not be repeated, although different samples were repeatedly recrystallized. Different specimens of jacobine and jaconine of varying rotation appeared to vary little in m.p. and always showed one spot

by paper chromatography, even when optically active acids (e.g. *d*-camphorsulphonic or *d*-tartaric) were substituted for acetic acid in the solvent.

Detection of Solvent of Crystallization in Jaconine and Its Hydrochloride and the Preparation of Solvent-Free Jaconine: A sample of jaconine hydrochloride when recrystallized from ethanol and dried under vacuum at 78 °C gave colourless needles, m.p. 205–206 °C (Found: C, 51.2; H, 7.2; N, 2.8; O, 23.6; Cl, 15.1; OEt, 7.8, 8.1%; loss in wt., nil. Calc. for $C_{20}H_{33}O_7NCl_2$: C, 51.5; H, 7.1; N, 3.0; O, 23.8; Cl, 15.1; OEt, 9.6%. Calc. for $C_{18}H_{27}O_6NCl_2$: C, 50.9; H, 6.4; N, 3.3; O, 22.6; Cl, 16.7%).

Jaconine recrystallized from ethanol and dried under vacuum at room temperature had m.p. 147–148 °C (Found: OEt, 5.2, 5.1%; loss in wt., nil. Calc. for $C_{20}H_{33}O_7NCl$: OEt, 10.4%). Jaconine recrystallized twice from methanol and dried under vacuum at room temperature had m.p. 148–149 °C (with effervescence) (Found: OMe, 3.0%). Jaconine recrystallized twice from carbon tetrachloride and dried under vacuum at 100 °C (Found: C, 55.8; H, 6.6; N, 3.2; O, 24.7; Cl, 9.3%. Calc. for $C_{18}H_{26}O_6NCl$: C, 55.7; H, 6.8; N, 3.6; O, 24.8; Cl, 9.1%. Calc. for $C_{20}H_{33}O_7NCl$: C, 55.4; H, 7.4; N, 3.2; O, 25.8; Cl, 8.2%).

(b) *Degradation of Jacobine and Jaconine.*—(i) *Alkaline Hydrolysis of Jacobine.* Jacobine (1.1 g), hydrated barium hydroxide (2.2 g), and water (12 ml) were heated at 100 °C for 2 hr. Carbon dioxide was passed until the solution was saturated and the barium carbonate was filtered. The filtrate acidified to Congo red with hydrochloric acid, was continuously extracted with ether for 4 hr, the ether removed, and the residues recrystallized from ethyl acetate gave colourless needles, m.p. 180 °C, $[\alpha]_D^{20} +29.1$ (c, 1.37 in water) (Found: C, 51.7; H, 6.9; CH_3C , 17.6, 17.5; equiv., 113%. Calc. for $C_{10}H_{14}O_6$: C, 51.7; H, 6.9; $3 \times CH_3C$, 19.4%; equiv., 116.1).

The aqueous acid layer after removal of the jaconic acid was evaporated to dryness *in vacuo*, and dried. It was extracted with three portions of boiling ethanol, and the filtrate on concentration to dryness gave crude retronecine hydrochloride (0.54 g), which recrystallized from ethanol gave colourless prisms, m.p. 162 °C (Found: C, 50.2; H, 7.4; Cl, 18.2%. Calc. for $C_8H_{14}O_2NCl$: C, 50.1; H, 7.4; Cl, 18.5%).

(ii) *Acid Hydrolysis of Jacobine and Preparation of the Chloro- and Bromodilactones.* Jacobine (0.35 g) was refluxed with 15% aqueous hydrochloric acid (2.5 ml) for 15 hr. The solution developed a reddish tinge and colourless crystals were observed in the condenser. These were collected (70 mg) and when sublimed at 100–120 °C/0.1 mm gave the *chlorodilactone* as a colourless solid, m.p. 112–113 °C, $[\alpha]_D^{20} -25.9^\circ$ (c, 1.31 in chloroform) (Found: C, 51.7; H, 5.7; O, 27.2; Cl, 15.6; act. H, 0.11%. Calc. for $C_{10}H_{12}O_4Cl$: C, 51.6; H, 5.6; O, 27.5; Cl, 15.2%). Zhdanovich and Men'shikov (loc. cit.) obtained a compound of this formula from the alkaloid othosenine having m.p. 111–113 °C and $[\alpha]_D -25.2^\circ$. Similarly, jacobine (1.65 g) and 48% hydrobromic acid (20 ml) yielded colourless crystals (1.24 g), which when sublimed at 125 °C/0.5 mm, and recrystallized from benzene-light petroleum gave long colourless needles, m.p. 117 °C, $[\alpha]_D^{19} -21.9^\circ$ (c, 1.96 in chloroform) (Found: Br, 28.5; CH_3C , 12.9%. Calc. for $C_{10}H_{12}O_4Br$: Br, 28.8; $2 \times CH_3C$, 10.8; $3 \times CH_3C$, 16.3%).

(iii) *Alkaline Hydrolysis of Jaconine.* Jaconine (0.34 g), hydrated barium hydroxide (0.68 g), and water (15 ml) were kept at 100 °C for 2 hr, and the procedure for extraction of the acid followed as above. The crude acid (0.18 g) when recrystallized from ethyl acetate gave colourless needles, m.p. 181–182 °C undepressed on admixture with the specimen of jaconic acid obtained above. The aqueous acid layer was evaporated to dryness, and the base hydrochloride isolated as before. It had m.p. 162–163 °C undepressed on admixture with the retronecine hydrochloride obtained above.

(iv) *Acid Hydrolysis of Jaconine.* Jaconine (1.06 g) was refluxed with aqueous 15% hydrochloric acid (20 ml) for 10 hr. On cooling, colourless plates (0.46 g) were obtained which were collected and recrystallized from benzene-light petroleum, to give colourless plates, m.p. 113–114 °C undepressed on admixture with the specimen obtained above. The aqueous solution after removal of the compound $C_{10}H_{12}O_4Cl$ was evaporated to dryness, the residue taken up in hot ethanol, and filtered. The filtrate taken to dryness gave retronecine hydrochloride, (0.668)

which from ethanol gave colourless prisms, m.p. 162 °C, alone or admixed with the retronecine hydrochloride obtained above.

Jaconine (0.63 g) was refluxed with 46–48% hydrobromic acid (7 ml) and water (7 ml) for 25 hr. Crystals collected in the condenser (0.1 g) which, when recrystallized from benzene-light petroleum gave colourless plates, m.p. 113–114 °C (Found: C, 51.8; H, 5.8%) undepressed when admixed with the chlorodilactone obtained above.

(v) *Hydrogenolysis of Jacobine*. Jacobine (0.70 g), platinum oxide (50 mg), acetic acid (5 ml), and ethanol (20 ml) were shaken in the presence of hydrogen for 1 hr when 2 mol. hydrogen were absorbed (no further absorption of hydrogen occurred after a further 5 hr shaking). After removal of the platinum and the solvent a white solid was obtained almost insoluble in ethanol, but soluble in acetic acid. It could not be satisfactorily crystallized, but had m.p. 212 °C (Found: C, 60.5; H, 8.0; N, 4.0%. Calc. for $C_{15}H_{20}O_6N$: C, 60.8; H, 8.2; N, 3.9%). It must therefore be the *internal salt monoester, retronecanol jaconecate*, and this is confirmed by hydrolysis, with barium hydroxide which by the usual procedure gave jaconecic acid and retronecanol, m.p. 95 °C (Found: C, 67.9; H, 10.9; N, 9.9%. Calc. for $C_8H_{11}ON$: C, 68.1; H, 10.7; N, 9.9%).

Hydrogenolysis of jaconine proceeded more slowly, 1 mol. hydrogen being absorbed after 2½ hr, and a white solid separated after 3½ hr, which had m.p. 190–191 °C, but could not be further purified. Hydrolysis of the product gave jaconecic acid as before.

(c) *Jaconecic Acid and Its Derivatives*.—(i) *Jaconecic Acid*. Jaconecic acid gave a colour with ferric chloride. Hydrogenation was unsuccessful, jaconecic acid being recovered unchanged; tetranitromethane gave a negative test. Jaconecic acid was recovered unchanged on refluxing with 15% hydrochloric acid.

(ii) *Oxidation of Jaconecic Acid with Lead Tetra-acetate*. The method of Christie *et al.* (1949) was followed. Glacial acetic acid (10 ml) and lead tetra-acetate (0.8 g) were placed in the reaction flask, and carbon dioxide bubbled through until the air was displaced. Water (1 ml) was quickly added, carbon dioxide passed again for a few minutes then shut off, and the outlet connected to a gas burette. The weighed jaconecic acid (0.245 g) suspended in a capsule above the liquid was then dropped into the reaction mixture. Carbon dioxide was immediately evolved and when the rate of evolution had slackened the flask was heated to 60 °C. After cooling carbon dioxide (23.1 ml. Calc. for 1 mol: 25.4 ml) was obtained.

(iii) *Acetyljaconecic Acid*. Jaconecic acid (0.28 g), acetyl chloride (0.35 ml), and dry freshly distilled acetone (5 ml) were refluxed for 1 hr. Removal of the solvent gave an oily residue which crystallized on standing. Recrystallized from ethyl acetate, acetyljaconecic acid formed long colourless prisms, m.p. 195–196 °C, $[\alpha]_D^{26} +9.1^\circ$ (c, 2.854 in ethanol) (Found: C, 52.6; H, 6.5; OAc, 16.2%; equiv., 139. Calc. for $C_{12}H_{14}O_7$: C, 52.5; H, 6.6; OAc, 15.7%; equiv., 137.1).

(iv) *Monoethyl Jaconecate*. The isolation of this compound will be described in a later section. Monoethyl jaconecate was obtained as a colourless oil, b.p. 142–143 °C/0.7 mm, $[\alpha]_D^{22} +34^\circ$ (c, 2.122 in ethanol) (Found: C, 55.2; H, 7.6; O, 36.8%; equiv., 269. Calc. for $C_{13}H_{20}O_6$: C, 55.4; H, 7.7; O, 36.9%; equiv., 260). Hydrolysis gave jaconecic acid, $[\alpha]_D^{20} +31^\circ$, m.p. 181–182 °C undepressed with authentic specimen.

(v) *Dimethyl Jaconecate*. Jaconecic acid (2.31 g) was treated with diazomethane (from nitrosomethylurea, 20.6 g) in ether (150 ml) and the solution allowed to stand 16 hr. Removal of the ether gave dimethyl jaconecate as an oil (2.78 g), b.p. 120–124 °C/0.7 mm, $[\alpha]_D^{20} +28.2^\circ$ (c, 1.914 in ethanol), $n_D^{19} 1.4614$, $d_4^{19} 1.158$, $[R_L]_D^{19} 61.7$ (calc. for dimethyl ester of formula X, 61.7) (Found: C, 54.9; H, 7.9; O, 36.7; CH_3O , 22.3%. Calc. for $C_{13}H_{20}O_6$: C, 55.4; H, 7.7; O, 36.9; CH_3O , 23.8%).

(vi) *Reduction of Dimethyl Jaconecate with Lithium Aluminium Hydride*. The dimethyl ester (2.17 g) in dry ether (100 ml) was added dropwise to a mixture of powdered lithium aluminium hydride (5 g) in dry ether (250 ml). The mixture was refluxed for 2 hr then allowed

to stand for 16 hr. Cold 10% aqueous sodium hydroxide (120 ml) was added cautiously to the cooled reaction mixture, the ether removed, and the aqueous phase continuously extracted with ether for 6 hr. Removal of the ether gave a viscous liquid (1.5 g) which failed to crystallize even after purification by passage through a column of alumina (100 g), developing with benzene-ether and ether-ethanol mixtures, and eluting with 50% ether-ethanol. It had $[\alpha]_D^{20} +23.1^\circ$. Benzoylation by the Schotten-Baumann procedure yielded an oil. A triacetate was prepared from the reduction product (8.5 g) and acetic anhydride (40 ml) by refluxing for 2 hr, removal of the excess acetic anhydride *in vacuo*, and finally, by standing in a desiccator over solid sodium hydroxide. It had b.p. 154–157 °C/1 mm, $[\alpha]_D^{25} +11.2^\circ$ (c, 2.69 in ethanol), $n_D^{25} 1.4553$ (Found: C, 58.0; H, 8.0%. Calc. for $C_{16}H_{24}O_7$: C, 58.2; H, 7.9%).

A *p*-nitrobenzoate was prepared from the reduction product (0.58 g), pyridine (20 ml), and *p*-nitrobenzoyl chloride (3 g). The mixture was allowed to stand for 16 hr, refluxed for 1 hr, cooled, taken up in ether, and the ether solution washed with cold dilute (1:4) aqueous hydrochloric acid, 5% aqueous sodium hydroxide, water, and then dried over sodium sulphate. Removal of the ether gave a solid (72 mg) which when recrystallized from ethanol gave fine colourless needles, m.p. 164 °C (Found: C, 57.4; H, 4.6; O, 31.5; N, 6.5%. Calc. for $C_{21}H_{25}O_{12}N_2$: C, 57.1; H, 4.5; O, 31.9; N, 6.5%).

(vii) *Oxidation with Periodic Acid.* Following the procedure of Jackson (1944), a quantitative determination showed that the reduction product consumed 0.90 ml periodic acid per mol. substance over a period of 17 hr. Steam distillation of the reaction mixture yielded formaldehyde identified as its dimerone derivative, m.p. 188–189 °C undepressed on admixture with an authentic specimen.

(viii) *Oxidation with Lead Tetra-acetate.* The reduction product (3.15 g) in glacial acetic acid (20 ml) was added to a hot solution of lead tetra-acetate (12.6 g) in glacial acetic acid (25 ml), and the mixture allowed to stand for 30 min. It was then steam distilled and the distillate collected in a solution of dimedone (4.0 g) in 30% aqueous ethanol (100 ml). Colourless needles (1.4 g), m.p. 191 °C undepressed with the dimedone derivative of formaldehyde were obtained.

(d) *Isolation of isoJaconecic Acid.*—Jacobine (52.6 g), ethanol (250 ml), and sodium hydroxide (15 g) in water (20 ml) were refluxed for 2 hr, and the ethanol distilled. The residue was cooled, and strongly acidified with conc. hydrochloric acid. The precipitated acid was filtered and dried separately and the filtrate was continuously extracted with ether. The total crude acid (35 g) was fractionally crystallized from ethyl acetate to give pure jaconecic acid, m.p. 181–182 °C, $[\alpha]_D^{26} +29^\circ$ (c, 1.93 in water) and an oily fraction from the mother liquors $[\alpha]_D^{23} +42.5^\circ$ (c, 1.98 in water), both products being obtained in approximately equal amounts. Paper chromatography, using butanol saturated with 5% aqueous acetic acid as the mobile phase, and spraying the dried paper with a saturated solution of bromeresol green showed that the oily fraction contained three compounds having R_F values of 0.92, 0.76, and 0.52. The crystalline jaconecic acid had R_F 0.52. The three components were separated by passage through a column of silica gel moistened with 0.5N sulphuric acid, using chloroform and chloroform-butanol mixtures for elution. The compound of R_F 0.92 was separated quite distinctly in the 5% butanol-chloroform eluate and shown to be the monoethyl jaconecate previously described. The 10% butanol-chloroform fractions contain firstly, the pure compound of R_F 0.76 (*isojaconecic acid*) then mixtures of this compound and jaconecic acid. *isoJaconecic acid* when first obtained from the column fractions is an oil but this crystallizes on standing. When sublimed at 180–220 °C/1.5 mm it is also obtained as a viscous liquid which on drying *in vacuo* over phosphorus pentoxide at 78 °C slowly solidifies and has m.p. 113–114 °C, $[\alpha]_D^{22} +74.8^\circ$ (c, 1.79 in ethanol) (Found: C, 51.9; H, 7.2; O, 41.5%; equiv., 119. Calc. for $C_{10}H_{16}O_6$: C, 51.7; H, 6.9; O, 41.3%; equiv., 116). It gives a faint colour with ferric chloride and is almost inert to periodic acid (Table 3). Attempted acetylation by the procedure previously used for jaconecic acid failed to give a crystalline product. *isoJaconecic acid* is recovered unchanged on refluxing with 15% hydrochloric acid. The *di-p*-phenylphenacyl derivative prepared in the usual way was obtained as colourless crystals, m.p. 154–155 °C (Found: C, 73.6; H, 5.9; O, 20.8%. Calc. for $C_{28}H_{28}O_8$: C, 73.5; H, 5.8; O, 20.6%).

(e) *Alkaline Hydrolysis of the Dilactone $C_{10}H_{12}O_4Cl$* .—The dilactone (1.78 g) was refluxed with sodium hydroxide (2 g) and water (10 ml) for 1 hr, made acid with hydrochloric acid, and the solution continuously extracted with ether. Distillation of the ether gave an oil (1.6 g) which, when recrystallized from ethyl acetate, gave colourless needles, m.p. 186 °C, $[\alpha]_D^{25} +42.4^\circ$ (c, 1.13 in water), undepressed on admixture with jaconecic acid.

In another experiment, the dilactone (2.85 g) in 100 ml ethanol was treated with 0.0862N sodium hydroxide (450 ml) and the solution slowly concentrated at 100 °C, *in vacuo*. An attempt was made to back-titrate the solution with 0.1N hydrochloric acid, but the end-point was not sharp. It was found that approximately 312 ml 0.100N sodium hydroxide was used (calc. for 3 equiv., 368 ml). The solution was finally made strongly acid with conc. hydrochloric acid and continuously extracted with ether. Evaporation of the ether gave a gum (2.70 g), $[\alpha]_D^{21} +36.7^\circ$ (c, 2.124 in water), showing three spots on paper at R_F 0.79, 0.76, and 0.52. The last two were due to *isojaconecic* and *jaconecic* acid respectively. Chromatography of the mixture on silica gel (300 g), moistened with 0.5N sulphuric acid (30 ml), using acetone-chloroform mixtures for elution yielded in the 10% acetone-chloroform eluate *jaconecic monolactone* (0.35 g) of R_F 0.79, which distilled at 120–140 °C (bath temp.)/1 mm as a colourless oil, $[\alpha]_D^{23} -10^\circ$ (c, 1.20 in water) (Found: C, 56.3; H, 6.8%; equiv., 233. Calc. for $C_{10}H_{14}O_5$: C, 56.1; H, 6.6%; equiv., 214). The 20% and 40% acetone-chloroform eluates yielded mixtures of *jaconecic* and *isojaconecic* acids from which *jaconecic* acid (0.75 g) could be separated in the pure state since it is much less soluble in chloroform than *isojaconecic* acid.

(f) *Jacozine and Its Derivatives*.—(i) *Hydrolysis of Jacozine*. Jacozine (0.32 g), hydrated barium hydroxide (0.64 g), and water (20 ml) were kept at 100 °C for 1.5 hr. Carbon dioxide was passed until the solution was saturated, the barium carbonate filtered, the filtrate made acid with conc. hydrochloric acid, and continuously extracted with ether for 8 hr. Distillation of the ether left an oil (0.15 g) which when recrystallized from ethyl acetate gave *Jacozineic acid* as colourless needles, m.p. 161 °C, $[\alpha]_D^{22} -29.7^\circ$ (c, 1.144 in ethyl acetate) (Found: C, 52.4; H, 6.5; CH_3C , 12.5%; equiv., 119. Calc. for $C_{10}H_{14}O_6$: C, 52.5; H, 6.1; $2 \times CH_3C$, 13.1%; equiv., 115.1). The aqueous acid solution after extraction with ether was evaporated to dryness, the residue extracted with hot ethanol, filtered, and the filtrate concentrated. Colourless prisms, m.p. 162 °C undepressed on admixture with retronecine hydrochloride was obtained.

(ii) *Acetyljacozineic Anhydride*. Jacozineic acid (0.64 g) was refluxed with acetyl chloride (5 ml) for 2 hr. The excess acetyl chloride was distilled and the residue recrystallized from acetone to give *acetyljacozineic anhydride* as colourless needles, m.p. 136 °C. The m.p. was not raised by recrystallization from ethyl acetate-light petroleum (Found: C, 57.0; H, 5.7; OAc, 16.5%. Calc. for $C_{12}H_{14}O_8$: C, 56.7; H, 5.5; OAc, 16.9%).

(g) *Jacoline and Its Derivatives*.—(i) *Hydrolysis of Jacoline*. Jacoline (1.77 g), hydrated barium hydroxide (3.5 g), and water (20 ml) were heated at 100 °C for 2 hr. Carbon dioxide was passed until saturated, the barium carbonate filtered off, and the filtrate acidified with hydrochloric acid. Continuous extraction with ether for 8.5 hr gave a viscous oil (0.5 g), which failed to crystallize. The solvent was removed and the residue was refluxed with acetyl chloride (5 ml) for 1 hr, the excess acetyl chloride removed, and the residue recrystallized from ethyl acetate. *Acetyljacolineic dilactone* formed long colourless needles (0.34 g), m.p. 159–160 °C, $[\alpha]_D^{20} +16.5^\circ$ (c, 1.09 in chloroform) (Found: C, 56.6; H, 6.2; OAc, 16.4; CH_3C , 15.2%. Calc. for $C_{12}H_{14}O_6$: C, 56.3; H, 6.3; $1 \times OAc$, 16.8; $2 \times CH_3C$, 11.7; $3 \times CH_3C$, 17.6%). The aqueous acid mother liquors from which the acids had been extracted were evaporated to dryness, the residue extracted with hot ethanol and concentrated. The base hydrochloride was obtained as colourless prisms, m.p. 162 °C undepressed on admixture with retronecine hydrochloride.

(ii) *Hydrolysis of Acetyljacolineic Dilactone*. This compound (0.746 g) was hydrolysed by heating at 100 °C with 0.1N sodium hydroxide (100 ml) for 3 hr. After that period the solution was concentrated somewhat *in vacuo* and an attempt made to back titrate with 0.1N hydrochloric acid. Approximately 40 ml was required but the end-point was very indistinct,

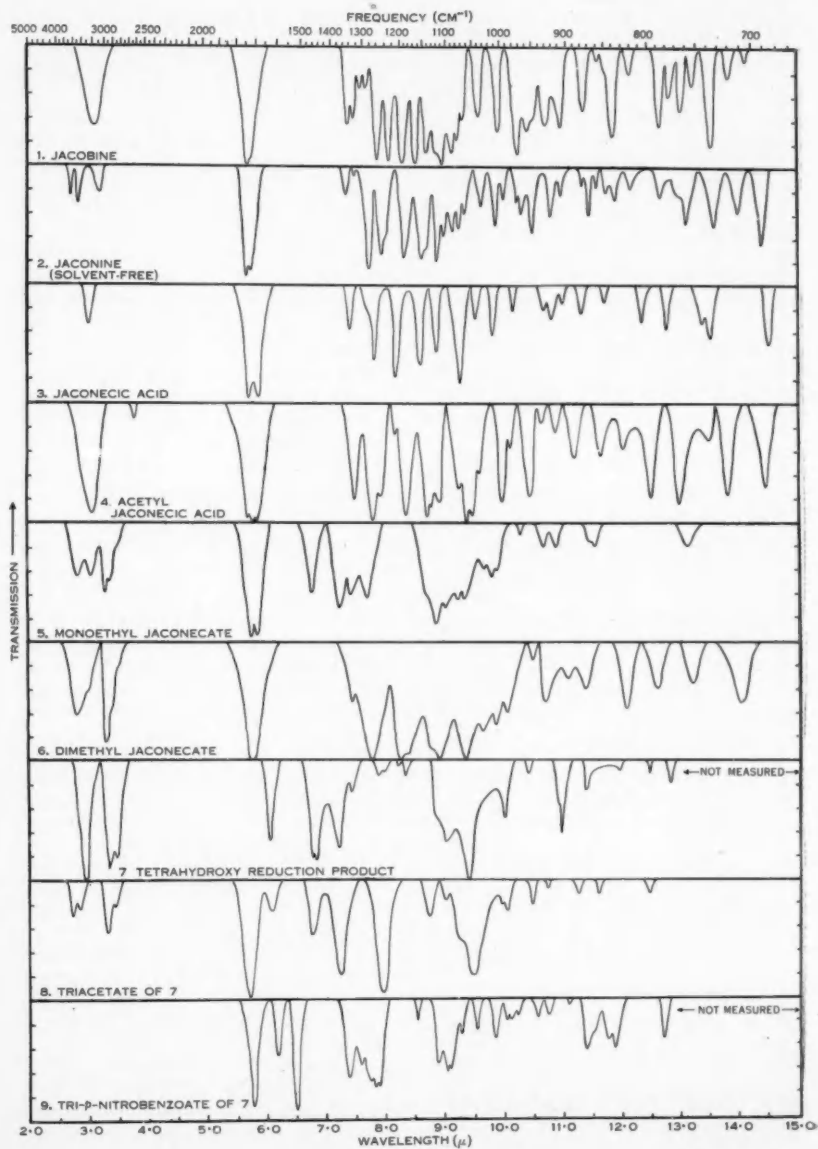


Fig. 1

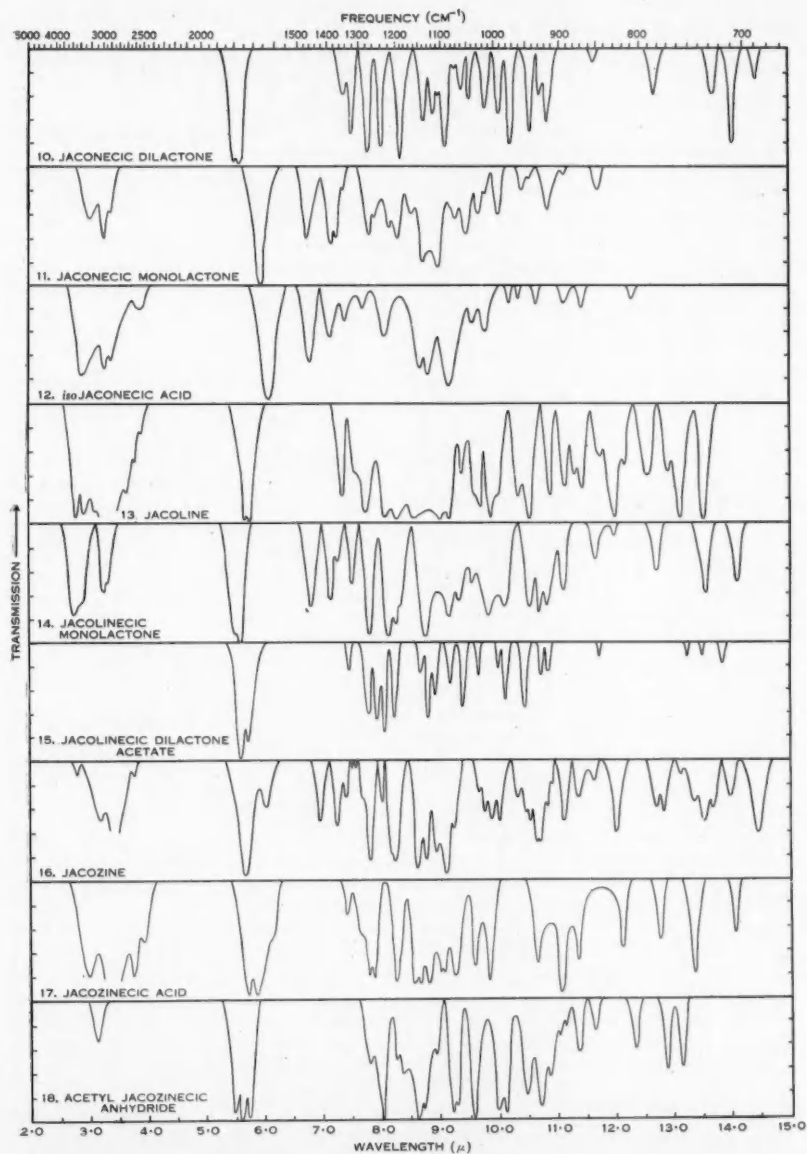


Fig. 1 (Continued)

and the solution which was made strongly acid with conc. hydrochloric acid (5 ml) was continuously extracted with ether for 8 hr. Removal of the ether gave jacolinecic monolactone as an oil (0.34 g), which distilled at 160–170 °C (bath temp.)/1 mm, showed only one spot on paper at R_F 0.83 (Table 3), and crystallized on standing m.p. 47 °C, $[\alpha]_D^{15}$ –21.7° (c, 2.86 in water) (Found: C, 55.8; H, 6.8; O, 37.0%; equiv., 246. Calc. for $C_{10}H_{14}O_5$: C, 56.1; H, 6.6; O, 37.3%; equiv., 214).

Spectroscopic Technique: The infra-red spectra were measured with a Perkin-Elmer model 12C spectrometer, converted to a double-pass instrument (Walsh 1952), and using a sodium chloride prism. Some of the substances were examined in the 3100–3700 cm^{-1} region with a calcium fluoride prism, which gives better resolution and more accurate frequency determination in this range.

Solid specimens were measured as mulls in "Nujol", though one substance, *isojaconecic* acid, would not form a satisfactory mull, and was studied as a vacuum-sublimed layer. Liquids were studied as thin films between a pair of rock salt plates. In Figure 1 are shown the spectra of the substances measured in this way. Since "Nujol" itself gives rise to strong absorption near 1380, 1460, and 3000 cm^{-1} there are small gaps in these regions.

Solutions in carbon tetrachloride or chloroform were measured in cells ranging from 0.05 to 2.0 cm in length. The solvents were of "AnalaR" quality and were not further purified, but were dried with silica gel before use. The 2% of ethanol in the chloroform was removed immediately before use by passage through a column of activated alumina.

IV. ACKNOWLEDGMENTS

The authors are indebted to Dr. R. H. F. Manske for a specimen of retronecic acid lactone and to Mr. L. Smith for specimens of senecic acid and its lactone. Valuable technical assistance was given by Messrs. F. Gori and S. Mosbauer.

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THE CHEMICAL CONSTITUENTS OF AUSTRALIAN *FLINDERSIA* SPECIES

IX. A SYNTHESIS OF FLINDERSINE*

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[Manuscript received October 24, 1955]

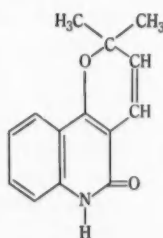
Summary

The alkaloid, flindersine, has been synthesized.

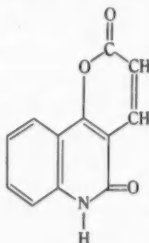
I. INTRODUCTION

In a previous communication (Brown *et al.* 1954) it was shown by degradative methods that the alkaloid flindersine had structure I. The present paper describes its synthesis.

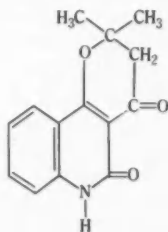
The method usually adopted for the preparation of polynuclear 2,2-dimethylpyrans is to react excess methyl magnesium iodide with the corresponding α -pyrone (Shriner and Sharp 1939). Substance II required for this reaction had previously been obtained by Asahina and Inubuse (1932) from 4-hydroxy-2-quinolone in several stages, but was more conveniently synthesized by heating 4-hydroxy-2-quinolone and malic acid with concentrated sulphuric acid. After a suspension of it in ether had been treated with methyl magnesium iodide it



(I)



(II)



(III)

was recovered quantitatively, and similar results were obtained when the Grignard reagent was added to a solution of the substance in anisole or dioxan. The failure of the reaction is attributed to the formation of a very sparingly soluble magnesium derivative of II.

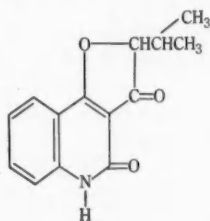
A second and successful route involved the Fries reaction. In some model experiments 4-acetoxy-2-quinolone (Ashley, Perkin, and Robinson 1930) was

* A short account of this work appears in *Chem. & Ind.* 1955: 1385.

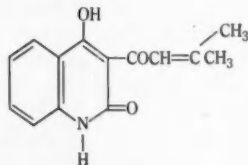
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treated with aluminium chloride in nitrobenzene solution below 20 °C. Some 4-hydroxy-2-quinolone was formed but a good yield of 3-acetyl-4-hydroxy-2-quinolone was recovered. Its structure was established by the observations: (i) that it formed a 2,4-dinitrophenylhydrazone, (ii) that acid hydrolysis gave acetic acid and a nearly quantitative yield of 4-hydroxy-2-quinolone, and (iii) that it was identical with the product of the reaction between aniline and acetylmalonic ester in either boiling nitrobenzene (Vaughan 1946) or diphenyl ether (Baker, Lappin, and Riegel 1946).

For the alkaloid synthesis, 4-hydroxy-2-quinolone was treated in suspension in pyridine with $\beta\beta$ -dimethylacryloyl chloride to yield the corresponding ester, which was then subjected to the action of aluminium chloride. As before, some 4-hydroxy-2-quinolone was isolated but the yield of the other product was small. It formed a 2,4-dinitrophenylhydrazone and hence could have been either III, IV, or V. It was formulated as III since in other examples of the



(IV)



(V)

Fries reaction with esters of $\beta\beta$ -dimethylacrylic acid it has been found that cyclization to a six-membered but not to a five-membered ring occurs, and that ketones of type V are very readily cyclized under mild acid conditions to substances of type III (Auwers and Lämmerhirt 1920; Bridge, Heyes, and Robertson 1937; Bridge *et al.* 1937). Catalytic hydrogenation of III gave the related alcohol which was further reduced by phosphorus and hydriodic acid to dihydroflindersine. The identity of this substance with that derived from the natural product was established by mixed m.p. determinations and by comparing the ultraviolet and infra-red spectra which were respectively identical. Dehydration of the alcohol to flindersine was effected by hot sulphuric acid (1:1), by phosphorus pentoxide in boiling benzene, or better by thionyl chloride in cold chloroform. The synthetic material melted a little higher than natural flindersine and did not give an anomalous methylenedioxy test under any conditions (Brown *et al.* 1954). However, after the latter had been purified by chromatographing its solution in ethyl acetate on alumina, the method used for synthetic flindersine, the two products were completely identical having the same m.p. and mixed m.p. and the same ultraviolet and infra-red spectra.

In Table 1 are given the ultraviolet absorption data for 4-hydroxy-2-quinolone, its 4-methyl ether, and the substances described above. Methylation of the hydroxyl group has little effect on the light absorption, and its acylation results merely in the coalescence of the small twin peaks at 270 and 280 m μ .

to a broad band and the absorption at slightly longer wavelengths in the region of 330 $m\mu$. The spectra of the alcohol and dihydroflindersine are similar to that of 4-hydroxy-2-quinolone, but the introduction of a carbonyl group (as in the ketones) or of an ethylenic residue (as in flindersine) at the 3-position eliminates the peaks at 270 and 280 $m\mu$ and shifts the absorption maxima to the region of 350 $m\mu$. This effect was noted previously (Brown *et al.* 1954).

TABLE I
ULTRAVIOLET ABSORPTION SPECTRA
In methanol

4-Hydroxy-2-quinolone	$\lambda_{\max.}$ ($m\mu$) Log $\epsilon_{\max.}$	230 4.19	270 3.96	280 3.94	316 3.83	
4-Methoxy-2-quinolone	$\lambda_{\max.}$ ($m\mu$) Log $\epsilon_{\max.}$	230 4.15	265 3.87	275 3.85	315 3.80	
4-Acetoxy-2-quinolone	$\lambda_{\max.}$ ($m\mu$) Log $\epsilon_{\max.}$	230 4.36	270 3.88	327 3.89		
4 β -Dimethylacryloxy-2-quinolone	$\lambda_{\max.}$ ($m\mu$) Log $\epsilon_{\max.}$	230 4.37	270 3.85	330 3.80		
3-Acetyl-4-hydroxy-2-quinolone	$\lambda_{\max.}$ ($m\mu$) Log $\epsilon_{\max.}$	230 4.38	245 4.26	300 4.12	350 3.71	
Ketone (III)	$\lambda_{\max.}$ ($m\mu$) Log $\epsilon_{\max.}$	230 4.42	290 3.95	302 3.96	350 3.62	
"Alcohol"	$\lambda_{\max.}$ ($m\mu$) Log $\epsilon_{\max.}$	225 4.50	272 3.88	281 3.88	316 3.81	
Flindersine	$\lambda_{\max.}$ ($m\mu$) Log $\epsilon_{\max.}$	235 4.42	333 4.00	350 4.10	365 3.93	
Dihydroflindersine	$\lambda_{\max.}$ ($m\mu$) Log $\epsilon_{\max.}$	225 4.44	272 3.94	283 3.96	312 3.93	
"Coumarin (I)"	$\lambda_{\max.}$ ($m\mu$) Log $\epsilon_{\max.}$	225 3.76	255 3.66	330 3.44	357 3.49	370 3.46

II. EXPERIMENTAL

Melting points are uncorrected. Analyses are due to Mr. F. C. Hall and ultraviolet absorption data to Dr. F. B. Strauss and Mr. F. Hastings, Dyson Perrins Laboratory, Oxford.

(a) *2'-Pyrono(5',6',3,4)-2-quinolone*.—Malic acid (15 g) was added to a solution of 4-hydroxy-2-quinolone (7.2 g) in warm concentrated sulphuric acid (36 ml) and the mixture heated on the water-bath with intermittent shaking to control the foaming. After 3 hr it was poured into a solution of sodium acetate (400 g) in water (1500 ml), the mixture boiled, and then allowed to stand overnight. The fine precipitate was collected, washed thoroughly, and then boiled with a solution of sodium bicarbonate (7.5 g) in water (500 ml). Undissolved material was filtered from the hot liquid, washed thoroughly, and dried. The substance was purified by crystallization from glacial acetic acid, sublimation at 280–300 °C/0.1 mm, and further crystallization

from glacial acetic acid. It (1.6 g, 16% yield) formed small dull pale yellow prismatic needles, m.p. 345–346 °C (Found: C, 67.4; H, 3.5%. Calc. for $C_{12}H_7O_2N$: C, 67.6; H, 3.3%). Asahina and Inubuse (1932) give m.p. 335 °C. It was very sparingly soluble in the usual organic solvents.

The alkaline filtrate was acidified while hot with acetic acid, the precipitate collected, washed with water, then acetone, and dried (2.0 g). Acetylation with acetic anhydride and pyridine (Ashley, Perkin, and Robinson 1930) gave eventually pure 4-acetoxy-2-quinolone (1.1 g).

(b) *3-Acetyl-4-hydroxy-2-quinolone*.—(i) A mixture of aniline (4.7 g; 0.05 mol), ethyl acetylmalonate (20 g; 0.1 mol), and nitrobenzene (75 ml) was heated in an oil-bath at 230–235 °C for 2 hr in a flask fitted with a short condenser so that the ethanol formed could escape. After cooling, the dark product was filtered off, washed with ether, and extracted with boiling 5% potassium carbonate (60 ml). The extract was treated with charcoal, filtered, and acidified with acetic acid. The precipitate was collected, washed, and recrystallized from glacial acetic acid giving the pure ketone (1.5 g, 15% yield) as very pale yellow prisms, m.p. 255–256 °C (slight decomp.) after sintering at about 245 °C (Found: C, 64.7; H, 4.5%. Calc. for $C_{11}H_7O_2N$: C, 65.0; H, 4.5%). It was sparingly soluble in the usual organic solvents and insoluble in boiling 5N hydrochloric acid. It was unaffected by acetic anhydride and pyridine at 100 °C for 30 min or by boiling 20% potassium hydroxide for 2 hr. It gave an orange ferric test with ethanolic ferric chloride.

The *2,4-dinitrophenylhydrazone* prepared by heating an ethanolic solution of the ketone with a solution of the reagent in ethanolic sulphuric acid on the water-bath, crystallized from nitrobenzene in small bright red prisms which effervesced at about 315 °C after previous gradual darkening (Found: N, 18.6%. Calc. for $C_{17}N_3O_6$: N, 18.3%).

(ii) A mixture of aniline (31 g; 0.33 mole), ethyl acetylmalonate (72 g; 0.33 mole), and diphenyl ether (175 ml) was heated in a flask fitted with a short condenser. A brisk reaction soon commenced and ethanol escaped from the top of the condenser. When the reaction slackened heating was resumed and, finally, the mixture was boiled vigorously. After a total heating time of 45 min the mixture was cooled, the product collected, washed with ether and purified as above. The yield was 15 g (22%) m.p. and mixed m.p. 255–256 °C.

(iii) Powdered aluminium chloride (14 g; 0.105 mole) was dissolved in pure dry nitrobenzene (100 ml) and the solution cooled in ice water. 4-Acetoxy-2-quinolone (8.1 g; 0.04 mole) was added in one lot and the mixture shaken. The resulting solution was kept below 20 °C for 40 hr and then shaken with ether and 3% hydrochloric acid. The precipitate was collected, washed, and boiled with 3N hydrochloric acid (300 ml). The crude ketone was filtered from the hot solution and purified by crystallization from glacial acetic acid, giving nearly colourless prisms (5.2 g, 65%), m.p. and mixed m.p. 255–256 °C.

By the addition of sodium acetate (150 g) to the hot acid filtrate, 4-hydroxy-2-quinolone (1.3 g), identified through its acetyl derivative, was recovered.

(c) *Hydrolysis of 3-Acetyl-4-hydroxy-2-quinolone*.—The ketone (4.5 g) was refluxed with water (22 ml) and concentrated sulphuric acid (22 ml) for 1 hr. The hot mixture was poured into a hot solution of sodium acetate (70 g) in water (500 ml) and the precipitate (3.6 g, 97%) collected, washed, and dried. It was completely soluble in hot 3N hydrochloric acid and was identified as 4-hydroxy-2-quinolone in the usual way.

(d) *4-ββ-Dimethylacryloxy-2-quinolone*.—A suspension of 4-hydroxy-2-quinolone (4.8 g; 0.03 mole) in dry pyridine (20 ml) at 0 °C was treated with ββ-dimethylacryloyl chloride (4.8 g; 0.04 mole) in one lot. The mixture was heated on the steam-bath until the solid had dissolved (about 1 hr), and then kept overnight. On the addition of dilute acetic acid a pasty precipitate formed which became granular on gentle warming. It was collected, washed thoroughly, and recrystallized from ethanol giving the pure ester (5.9 g, 80%) as colourless needles, m.p. 214 °C after sintering at about 200 °C (Found: C, 69.3; H, 5.5%. Calc. for $C_{14}H_{13}O_2N$: C, 69.1; H, 5.4%).

(e) *2',2'-Dimethyl-2',3'-dihydro-4'-pyrano(5',6',3,4)-2-quinolone*.—The ester (9.6 g; 0.04 mole) was added to a solution of aluminium chloride (14.6 g; 0.11 mole) in nitrobenzene (100 ml)

cooled in ice water and the resulting reddish brown solution kept below 20 °C for 40 hr. The solution was diluted with chloroform and ammonium chloride (50 g) in water (200 ml) added. On shaking, a crystalline precipitate formed, which was collected, washed, and dried (2.0 g). It was identified in the usual way as 4-hydroxy-2-quinolone. The organic layer was separated from the filtrate and the solvents removed by a current of steam. The residue was thoroughly extracted with chloroform, the extracts dried and evaporated. The dark crystalline material on repeated crystallization from ethyl acetate containing a little methanol gave the *ketone* (3.0 g, 30%) as colourless leaflets, m.p. 247 °C with darkening commencing at about 200 °C (Found: C, 69.2; H, 5.4%. Calc. for $C_{14}H_{13}O_2N$: C, 69.1; H, 5.4%). It gave an orange ferric test.

The 2,4-dinitrophenylhydrazone prepared as in Section II (b) (i) crystallized from nitrobenzene in small bright red needles which effervesced at 295–297 °C after slight previous darkening (Found: N, 16.2%. Calc. for $C_{20}H_{17}O_9N_5$: N, 16.5%).

(f) *Reduction of the Ketone*.—A warm suspension of the ketone (1 g) and platinum oxide (0.1 g) in ethanol (50 ml) was shaken at atmospheric pressure with hydrogen. After about 30 min, approximately the theoretical amount of hydrogen had been absorbed and uptake ceased. The catalyst was filtered off, the filtrate evaporated to dryness, and the crystalline residue recrystallized from ethyl acetate. The *alcohol* (0.8 g, 80%) formed colourless needles, m.p. 209 °C (slight decomp.) (Found: C, 68.5; H, 6.0%. Calc. for $C_{14}H_{15}O_2N$: C, 68.6; H, 6.2%). It gave an orange ferric test.

(g) *Dihydroflindersine*.—A mixture of the alcohol (0.2 g), red phosphorus (0.4 g), and concentrated hydriodic acid (12 ml) was refluxed for 2 hr, then cooled, diluted and extracted with chloroform. The residue from the evaporation of the solvent was purified by chromatographing its solution in ethyl acetate on alumina. The product (0.08 g, 40%) crystallized from ethyl acetate in colourless hexagons, m.p. 233 °C (very slow heating) or m.p. 227 °C with marked sintering at 205 °C (rapid heating) (Found: C, 73.6; H, 6.6%. Calc. for $C_{14}H_{15}O_2N$: C, 73.3; H, 6.6%). Authentic dihydroflindersine purified in the same manner behaved in the same way as did a mixture of the two samples.

(h) *Flindersine*.—(i) A solution of the alcohol (0.3 g) in 1:1 sulphuric acid (3 ml) was heated on the steam-bath for 20 min. After cooling, it was diluted and extracted with benzene, much amorphous material remaining undissolved. The extract was evaporated and the residue chromatographed in ethyl acetate on alumina. The product (0.025 g, 10%) crystallized from ethyl acetate in colourless needles, m.p. 195–196 °C (decomp.) on rapid heating or m.p. 189–190 °C (decomp.) on slow heating (Found: C, 74.0; H, 5.8%. Calc. for $C_{14}H_{15}O_2N$: C, 74.0; H, 5.8%). Natural flindersine purified by the same procedure showed the same behaviour as did also a mixture of the two samples. Catalytic reduction of the synthetic material (Brown *et al.* 1954) gave dihydroflindersine identical with the derivative from natural flindersine.

(ii) A solution of the alcohol (0.5 g) in dry benzene (25 ml) was refluxed with phosphorus pentoxide (1 g) for 45 min. The mixture was cooled, diluted with benzene, and shaken with dilute ammonia. The organic layer was washed, dried, and evaporated. The residue on purification as above gave flindersine (0.3 g, 65%).

(iii) Thionyl chloride (0.85 g) in pure dry chloroform (5 ml) was added in one lot to a solution of the alcohol (1.35 g) in chloroform (10 ml) containing a few drops of pyridine, cooled in an ice-bath. After 1 hr the mixture was removed from the bath and kept below 20 °C for 48 hr during which time a colourless crystalline precipitate gradually separated. The mixture was shaken with water, the chloroform layer separated, dried and evaporated. The residue on purification as above gave flindersine (0.9 g, 70%).

III. ACKNOWLEDGMENTS

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THE CHEMICAL CONSTITUENTS OF *HIMANTANDRA* SPECIES

II. THE ISOLATION OF THE ALKALOIDS OF *HIMANTANDRA* *BACCATA* BAIL. AND *H. BELGRAVEANA* F. MUELL.

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Summary

Ten new alkaloids have been isolated from the barks of *Himantandra baccata* Bail. and *H. belgraveana* F. Muell.

I. INTRODUCTION

The genus *Himantandra* is a rich source of various substances of phytochemical interest. In addition to the four new lignans whose isolation and structural determination were previously described (Hughes and Ritchie 1954), there are present sesquiterpenes and alkaloids. The structure of one sesquiterpene alcohol, himbacol, from *H. baccata* Bail. has been determined (Birch and Mostyn 1955) and work on other terpinoids will be reported later. The present paper describes the isolation of the alkaloids.

The study of the alkaloids was rendered difficult by the extreme variability of the alkaloid content of both *H. baccata* and *H. belgraveana* F. Muell. Samples collected in the same area and at approximately the same season have varied with respect to both the yield of total alkaloid and the individual alkaloids present. The north Queensland species, *H. baccata* was found to contain the three lignans, galbulin, galeatin, and galbacin, while *H. belgraveana* from New Guinea contained a fourth lignan, galgravin. The distinction between the two species based on alkaloid content was not so marked. Some alkaloids did appear to be confined to *H. baccata* and others to *H. belgraveana*, but owing to difficulties in separation it was not possible to be certain of this.

The alkaloids isolated from *H. baccata* have been named and assigned formulae as follows: himandrine, $C_{30}H_{37}O_6N$; himandridine, $C_{30}H_{37}O_7N$; himbacin, $C_{22}H_{35}O_2N$; himgravine, $C_{22}H_{33}O_2N$; himbadine, $C_{21}H_{31}O_2N$; and himbosine, $C_{45}H_{45}O_{13}N$ (?). Himbacin and himbadine occurred most regularly in reasonable yield, himandrine and himandridine were of more variable occurrence, himgravine was isolated from only one sample, and himbosine was isolated in very small yield.

H. belgraveana yielded himandrine, himbacin, himandrelene, $C_{32}H_{41}O_7N$; himgravine, $C_{22}H_{33}O_2N$; himbeline, $C_{22}H_{35}O_2N$; himandravine, $C_{21}H_{33}O_2N$;

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and himgrine, $C_{22}H_{33}O_3N$. The occurrence of himandrine was again very variable, the yield being either quite high or nil. When himandrine was not present, the major constituent was himgravine. The yield of himbeline was variable.

The method used for the separation of the alkaloids from large quantities (100–300 g) of the crude mixed alkaloids involved, firstly, the partition of the hydrochlorides between chloroform and 4 per cent. hydrochloric acid. This achieved a rough separation of himandrine, himbacine, himbeline, himgravine, himandravine, and himbosine, which form chloroform-soluble hydrochlorides, from himandridine, himandreline, himbadine, and himgrine. The individual alkaloids were then separated by chromatography and fractional crystallization. In every case, however, uncrystallizable residues remained and these could only be resolved into crystalline components by countercurrent distribution between phosphate buffer (pH 5.0–6.0) and light petroleum-benzene.

Inspection of the formulae of the alkaloids shows that the two main groups are present. Alkaloids of the formula $C_{22}H_{33-35}O_{2-3}N$ form the larger group and all four appear to be closely related, as do also the three more highly oxygenated alkaloids $C_{30-32}H_{37-41}O_{6-7}N$. The latter group is probably related to the former since preliminary experiments have shown that they are esters. Himbosine, himbadine, and himandravine at present do not appear to be closely related to either group.

II. EXPERIMENTAL

Melting points are uncorrected. Analyses are by Miss B. Stevenson and by C.S.I.R.O. Microanalytical Laboratory. Light petroleum refers to the fraction of b.p. 60–90 °C.

(a) *General Method of Isolation of the Alkaloids.*—The shade-dried milled bark was exhausted with cold methanol, the extract concentrated, basified with dilute sodium hydroxide and extracted with ether. The dark aqueous alkaline solution yielded no crystalline material and was discarded. The alkaloids were extracted from the ether solution with 4% hydrochloric acid, leaving a solution containing lignans and terpenoids (Hughes and Ritchie 1954). The acid extract was washed with ether, basified with ammonia, and the liberated bases extracted with chloroform. Evaporation of the solution gave a thick brown oil, which was dissolved in 4% hydrochloric acid (300 ml per 100 g of bases), and the solution extracted with chloroform (2 × 100 ml per 100 g). In this way the alkaloids whose hydrochlorides were soluble in chloroform (himandrine, himbacine, himbeline, himgravine, himandravine, and himbosine) were separated from those whose hydrochlorides were insoluble in chloroform (himandridine, himandreline, himbadine, and himgrine).

The chloroform solution was evaporated to dryness and the residue stirred with absolute ethanol. On standing crystalline himandrine hydrochloride separated and was collected. The filtrate was evaporated, basified with ammonia, and the bases extracted with chloroform. Chromatography of these bases in light petroleum on alumina then gave himbacine, himgravine, or himandravine depending on which was the major constituent of the sample. The other alkaloid could usually be obtained by rechromatographing the mother liquors and recrystallizing from light petroleum. A small yield of himbosine was occasionally obtained from the final mother liquors. In separating the alkaloids from *H. belgraveana*, himbeline was obtained as the minor constituent as a colourless gum. However, a crystalline hydrochloride was precipitated by saturating its solution in a little absolute ethanol with dry hydrogen chloride.

All the mother liquors from these operations were then combined and the uncrystallizable mixture of bases resolved by countercurrent distribution between 1M phosphate buffer of pH 5.0 to 6.0 and light petroleum containing 5–25% benzene. A 25-tube apparatus of the type described by Lathe and Ruthven (1951) was employed and their method of withdrawal was used to increase

the number of transfers beyond 24. Benzene was added to the light petroleum in order to increase the solubility of some mixtures and the buffer was chosen in order to give a partition coefficient close to 1.0. The amount of alkaloid in each tube after the distribution was determined by basifying the aqueous layers with sodium hydroxide, shaking and titrating 1 ml portions of the light petroleum layer with N/100 *p*-toluenesulphonic acid in chloroform, using methyl red in chloroform as the indicator. Further amounts of himbaine, himbaine, and himbaine were obtained by working up the tubes corresponding to peaks in the distribution curve.

The acid solution of the bases with chloroform-insoluble hydrochlorides was basified and the bases extracted with chloroform. After evaporation of the chloroform the residue was stirred with light petroleum containing some benzene when crude himandrine crystallized. Recrystallization of the bases in the mother liquors from 80% aqueous methanol gave crystalline himbaine hydrate. The mother liquors from these operations were then subjected to counter-current distribution, as described above, when further quantities of himandrine and himbaine were usually obtained. In addition two minor alkaloids, himandreline and himgrine, were obtained in this way from one sample of *H. belgraveana* bark.

(b) *Extractions of H. baccata Bark.*—(i) Sample A (80 kg), collected near Boonjie, north Queensland, in August 1947 (C.S.I.R.O. sample No. 4273), was extracted as above. The chloroform-soluble hydrochloride fraction yielded himandrine (56 g, 0.07%), himbaine (32 g, 0.04%), himbaine (5 g, 0.006%), and himbaine (0.4 g, 0.0005%). Himandrine (20 g, 0.025%) and himbaine (10 g, 0.012%) were obtained from the chloroform-insoluble hydrochloride fraction. A large uncrystallizable residual fraction (180 g) was later treated by countercurrent distribution.

(ii) Sample B (58 kg) was collected near Boonjie in November 1949 (C.S.I.R.O. sample No. 4589). The chloroform-soluble hydrochloride fraction yielded himbaine (12 g, 0.021%) and himbaine (0.1 g) while the chloroform-insoluble hydrochloride fraction gave himandrine (20 g, 0.035%) and himbaine (10 g, 0.017%). Uncrystallizable mixed bases (80 g) remained.

(iii) Sample C (73 kg), collected near Boonjie in September 1953 (C.S.I.R.O. sample No. 5272), yielded himbaine (12 g, 0.016%) and himbaine (22 g, 0.03%).

(iv) Sample D (45 kg), collected near Boonjie in July 1954 (C.S.I.R.O. sample No. 5477), gave only a very small amount of total alkaloid. This yielded himandrine (1 g, 0.002%) and himandrine (1 g, 0.002%).

(v) Sample E (76 kg), collected near Boonjie in September 1954 (C.S.I.R.O. sample No. 5478) gave himbaine (85 g, 0.11%), himandrine (6 g, 0.008%), and himbaine (9 g, 0.012%).

(c) *Extractions of H. belgraveana Bark.*—(i) Sample A (13 kg) was collected at Aiyura on the eastern highlands of New Guinea in August 1951 (C.S.I.R.O. sample No. 5091). It yielded himandrine (47 g, 0.36%) and himbaine hydrochloride (4 g, 0.03%).

(ii) Sample B (42 kg), collected at Aiyura in November 1952 (C.S.I.R.O. sample No. 5479), gave only himbaine (41 g, 0.095%).

(iii) Sample C (47 kg), collected at Aiyura in July 1954 (C.S.I.R.O. sample No. 5480), gave a chloroform-soluble hydrochloride fraction which yielded himbaine (18 g, 0.039%) and himbaine hydrochloride (6 g, 0.013%). Countercurrent distribution of the chloroform-insoluble hydrochloride fraction separated two minor alkaloids, himandreline (0.2 g, 0.0004%) and himgrine (3.5 g, 0.007%).

(iv) Sample D (23 kg) (C.S.I.R.O. sample No. 5397), for which no details of collection are available, gave himbaine (55 g, 0.24%), himandrine (17 g, 0.074%), and himbaine (5 g, 0.022%).

(d) *Himandrine.*—Himandrine crystallized from ethanol in thick colourless prisms and from aqueous ethanol as glistening leaflets, m.p. 185–186 °C, $[\alpha]_D^{20} -38^\circ$ (c, 1.22% in chloroform) (Found: C, 71.0; H, 7.3; O, 18.4; N, 2.8; OCH₃, 12.7%; (N)CH₃, nil. Calc. for C₃₀H₃₇O₈N: C, 71.0; H, 7.4; O, 18.9; N, 2.8; 2 × OCH₃, 12.2%).

The hydrochloride, which was sparingly soluble in cold water or ethanol, formed small colourless needles, m.p. 222 °C (decomp.) (Found: C, 66.7; H, 7.1; N, 2.6; Cl, 6.9%. Calc. for C₃₀H₃₈O₈NCl: C, 66.2; H, 6.9; N, 2.6; Cl, 6.5%).

The *hydriodide*, which could be obtained either by precipitation of a solution of the alkaloid in dilute sulphuric acid with potassium iodide or by heating the alkaloid with excess methyl iodide at 100 °C for 2 hr, formed small colourless prisms from ethanol, m.p. 201–202 °C (Found: C, 57.0; H, 5.9; N, 2.2%. Calc. for $C_{30}H_{38}O_6NI$: C, 56.7; H, 6.0; N, 2.2%).

The *methosulphate*, prepared by heating the alkaloid with one equivalent of dimethyl sulphate in dry benzene for 4 hr, formed small colourless prisms, m.p. 202 °C (Found: C, 60.2; H, 6.8%. Calc. for $C_{32}H_{40}O_{10}NS$: C, 60.6; H, 6.8%).

(e) *Himandridine*.—*Himandridine* crystallized from aqueous methanol or from benzene-light petroleum in colourless prisms, m.p. 204–205 °C, $[\alpha]_D^{18} - 22^\circ$ (c, 2.0% in chloroform) (Found: C, 68.8; H, 6.9; O, 20.9; N, 2.7; OCH_3 , 11.6%; $(N)CH_3$, nil. Calc. for $C_{30}H_{38}O_7N$: C, 68.8; H, 7.1; O, 21.4; N, 2.7; $2 \times OCH_3$, 11.9%).

The *hydriodide* obtained by heating with methyl iodide at 100 °C formed colourless needles from ethanol-ether, m.p. 194–195 °C (Found: C, 55.1; H, 6.2; I, 19.2%. Calc. for $C_{30}H_{38}O_7NI$: C, 55.3; H, 5.9; I, 19.6%).

(f) *Himandreline*.—*Himandreline* formed colourless prisms from benzene-light petroleum, m.p. 189–190 °C, $[\alpha]_D^{14} - 12^\circ$ (c, 1.01% in chloroform) (Found: C, 69.5; H, 7.4; N, 2.5; OCH_3 , 11.5%; $(N)CH_3$, nil. Calc. for $C_{32}H_{41}O_7N$: C, 69.7; H, 7.5; N, 2.5; $2 \times OCH_3$, 11.3%).

(g) *Himbosine*.—*Himbosine* crystallized from a large volume of methanol in colourless plates m.p. 262 °C, $[\alpha]_D^{15} + 55^\circ$ (c, 0.89% in chloroform) (Found: C, 65.8; H, 5.8; N, 1.8; OCH_3 , 4.8%. Calc. for $C_{43}H_{45}O_{13}N$: C, 65.7; H, 5.8; N, 1.8; $1 \times OCH_3$, 4.0%).

(h) *Himgravine*.—*Himgravine* crystallized from light petroleum in small colourless needles, m.p. 120 °C, $[\alpha]_D^{18} + 47^\circ$ (c, 1.5% in chloroform) (Found: C, 77.0; H, 9.4; N, 4.1%. Calc. for $C_{22}H_{28}O_2N$: C, 76.9; H, 9.7; N, 4.1%).

The *methiodide*, which formed very readily at room temperature, crystallized from water in colourless needles, m.p. 191–192 °C (Found: C, 55.3; H, 7.4; I, 24.6%. Calc. for $C_{23}H_{30}O_2NI \cdot H_2O$: C, 54.9; H, 7.6; I, 25.1%).

(i) *Himbacine*.—*Himbacine* crystallized from heptane in large glistening needles, m.p. 132 °C, $[\alpha]_D^{14} + 63^\circ$ (c, 1.04% in chloroform) (Found: C, 76.5; H, 10.4; N, 4.1; $(N)CH_3$, 4.8%. Calc. for $C_{22}H_{28}O_2N$: C, 76.5; H, 10.2; N, 4.1; $(N)CH_3$, 4.4%).

The *hydrochloride* separated from acetone-ether in colourless rods, m.p. 267 °C (Found: C, 66.3; H, 9.5; N, 3.4; Cl, 8.5%. Calc. for $C_{22}H_{28}O_2NCl \cdot H_2O$: C, 66.0; H, 9.6; N, 3.5; Cl, 8.9%).

The *aurchloride* crystallized from ethanol as yellow needles, m.p. 125–127 °C (Found: C, 38.7; H, 5.5; N, 2.1; Au, 28.1%. Calc. for $C_{22}H_{28}O_2NAuCl_4$: C, 38.5; H, 5.3; N, 2.0; Au, 28.8%).

(j) *Himbeline*.—This alkaloid was always isolated as the *hydrochloride* which crystallized from ethanol in colourless needles, m.p. 265–266 °C (Found: C, 66.3; H, 9.4; N, 3.5; Cl, 8.9%. Calc. for $C_{22}H_{28}O_2NCl \cdot H_2O$: C, 66.1; H, 9.6; N, 3.5; Cl, 8.9%).

The regenerated base, after passage of its solution in light petroleum through a short column of alumina, crystallized from light petroleum in colourless needles, m.p. 100 °C, $[\alpha]_D^{18} + 19^\circ$ (c, 2.4% in chloroform) (Found: C, 76.4; H, 10.0; N, 4.2%. Calc. for $C_{22}H_{28}O_2N$: C, 76.5; H, 10.2; N, 4.1%).

The *methiodide*, formed as a gum by keeping the base with excess methyl iodide, crystallized on stirring with acetone. It separated from ethanol-ether in colourless needles, m.p. 216–217 °C (Found: C, 54.9; H, 7.7; I, 24.8%. Calc. for $C_{23}H_{30}O_2NI \cdot H_2O$: C, 54.7; H, 8.0; I, 25.1%).

(k) *Himgrine*.—The base has not been obtained crystalline but the *perchlorate* crystallized from aqueous ethanol in fine colourless needles, m.p. 143–144 °C (Found: C, 55.4; H, 7.3; N, 2.9; Cl, 7.0; $(N)CH_3$, 3.1%. Calc. for $C_{22}H_{34}O_7NCl \cdot H_2O$: C, 55.3; H, 7.6; N, 2.9; Cl, 7.4; $1 \times (N)CH_3$, 3.1%).

The *methiodide* crystallized from ethanol in colourless needles, m.p. 222–223 °C (Found: C, 55.3; H, 7.3%. Calc. for $C_{22}H_{36}O_3NI$: C, 55.1; H, 7.2%).

(l) *Himbadinine*.—*Himbadinine* crystallized from 80% aqueous methanol in large needles, which were obviously hydrated, and which softened and melted from 110 to 114 °C, $[\alpha]_D^{25} -4.2^\circ$ (c, 1.43% in chloroform) (Found (after drying at 50 °C): C, 74.6; H, 9.6; N, 4.3; O, 12.0; (N)CH₃, 4.3%. Calc. for $C_{21}H_{31}O_2N \cdot \frac{1}{2}H_2O$: C, 74.6; H, 9.5; N, 4.1; O, 11.8; (N)CH₃, 4.4%. Found (after drying at 110 °C/0.1 mm): C, 77.2; H, 9.2; O, 9.6%. Calc. for $C_{21}H_{31}O_2N$: C, 76.6; H, 9.5; O, 9.7%). *Himbadinine* was unstable in solution; alcoholic solutions on exposure to light and air darkened and acquired a pronounced violet fluorescence.

The *methiodide* which formed readily at room temperature, crystallized from methanol in small colourless rhombs, m.p. 247–249 °C (Found: C, 56.2; H, 7.2; N, 2.8; I, 26.5%. Calc. for $C_{22}H_{34}O_2NI$: C, 55.8; H, 7.2; N, 3.0; I, 26.8%).

The *methosulphate* obtained by heating the base with one equivalent of dimethyl sulphate in benzene, crystallized from ethanol-ether in fine colourless needles, m.p. 237–238 °C (Found: C, 60.8; H, 8.3; S, 7.2%. Calc. for $C_{22}H_{37}O_6NS$: C, 60.6; H, 8.2; S, 7.0%).

The *perchlorate* crystallized from ethanol-ether in small shining needles, m.p. 239 °C (Found: C, 58.3; H, 7.4%. Calc. for $C_{21}H_{32}O_6NCl$: C, 58.8; H, 7.5%).

(m) *Himandravine*.—*Himandravine* separated from hexane as fine colourless needles, m.p. 119 °C, $[\alpha]_D^{18} +23^\circ$ (c, 1.89% in chloroform) (Found: C, 76.3; H, 10.3; N, 4.3%; (N)CH₃, nil. Calc. for $C_{21}H_{32}O_2N$: C, 76.1; H, 10.0; N, 4.2%).

The *hydrochloride* prepared by passing a stream of dry hydrogen chloride into a solution of the base in dry ethanol, crystallized from acetone-ethanol in colourless prisms, m.p. 238–240 °C (Found: C, 68.2; H, 9.4; N, 3.4; Cl, 10.0%. Calc. for $C_{21}H_{34}O_2NCl$: C, 68.5; H, 9.3; N, 3.8; Cl, 9.6%).

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THE CHEMISTRY OF ANTS

I. TERPENOID CONSTITUENTS OF SOME AUSTRALIAN IRIDOMYRMEX SPECIES

By G. W. K. CAVILL,* D. L. FORD,* and H. D. LOCKSLEY*

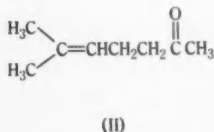
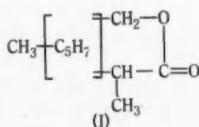
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Summary

Terpenoid constituents have been isolated from the following *Iridomyrmex* ants. The known methylheptenone (II) and iridodial, a novel dialdehyde ($C_{10}H_{16}O_2$), have been extracted from *Iridomyrmex detectus* (F.Sm.) and from *I. conifer* (Forel). *I. nitidus* (Mayr.) has yielded iridolactone ($C_{10}H_{16}O_2$). Iridodial is converted into iridolactone by the action of alkali. The isolation of iridomyrmecin (a lactone, $C_{10}H_{16}O_2$) from *I. humilis* (Mayr.) confirms the original observation of Pavan (1949).

I. INTRODUCTION

Numerous species of ants, particularly those of the subfamilies Dolichoderinae and Formicinae, including some of considerable economic importance, are reported to use odoriferous secretions and excretions in attack and defence against other species of ants and insects. Such odoriferous principles may also be employed in the laying of odour trails from food to nest (Wigglesworth 1950). However, few investigations concerned with the chemistry of ants have been described. The work of Stumper (1922*a*, 1922*b*, 1923, 1952*a*) on the secretion of formic acid by various species (over 40) of the subfamily Formicinae is well known. In addition, Stumper (1922*b*) had noted the absence of this acid from the four species of the subfamily Myrmecinae and from the one species of the Dolichoderinae which he examined. More recently, Stumper (1952*b*) suggested that some dolichoderines possess terpenoid odours, but no products were characterized.



The isolation of a terpenoid lactone, iridomyrmecin, from the anal glands of the Argentine Ant, *Iridomyrmex humilis* (Mayr.) (subfamily: Dolichoderinae) has been reported (cf. Pavan 1955). Previously, Pavan (1949, 1950) had shown that iridomyrmecin possessed antibiotic and insecticidal activity, and hence interest has been aroused in the chemistry of insects. The partial structure I has been proposed for iridomyrmecin (Fusco, Trave, and Vercellone 1955).

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2-Methylhept-2-en-6-one (II) has been detected as a steam-volatile constituent of the meat ant, *I. detectus* (F.Sm.) (Cavill and Ford 1953) and we now report on the further examination of this and related Australian *Iridomyrmex* species.

II. THE CONSTITUENTS OF *I. DETECTUS* (F.Sm.), *I. CONIFER* (FOREL),
I. NITIDUS (MAYR.), AND *I. HUMILIS* (MAYR.)

I. detectus is a common Australian species; the ants employed in the present investigation were collected near Canberra. A preliminary examination by steam distillation of an ant pulp, formed on maceration of the ants in aqueous suspension, yields methylheptenone (II) (Cavill and Ford loc. cit.). On several occasions 2-methylheptan-2-ol-6-one, isolated as the 2,4-dinitrophenylhydrazone, has also been obtained.

Solvent extraction of the whole ants with light petroleum gives a pale amber oil with the same characteristic odour as the steam distillate. On fractional distillation, under reduced pressure, this oil yields methylheptenone and a dicarbonyl compound, $C_{10}H_{16}O_2$, which we have named iridodial. Cholesterol has been isolated from the remaining fat fraction.

The methylheptenone has been characterized as the semicarbazone and 2,4-dinitrophenylhydrazone. Paper chromatography of the 2,4-dinitrophenylhydrazone precipitate, formed from the crude methylheptenone, obtained by solvent extraction of whole ants, confirmed the presence of this ketone. Methylheptanolone was not detected in this material and, hence, may be an artefact resulting from the steam-distillation process.

Iridodial is obtained as a colourless, optically active oil, b.p. 90–92 °C/1.0 mm, which readily polymerizes to a glassy mass. Distillation of the polymer, under reduced pressure, regenerates the monomer. Iridodial, which gives a blue colour on standing with Schiff's reagent, has been characterized as a yellow bis-2,4-dinitrophenylhydrazone and a di-semicarbazone. The attempted formation of a dimedone derivative gave a gum. Oxidation with potassium permanganate solution yields a dicarboxylic acid, $C_{10}H_{16}O_4$, isolated as the di-*p*-bromophenacyl ester, hence both carbonyl functions are aldehydic. The occurrence of such a terpenoid dialdehyde in Nature is novel.

The stick ant, *I. conifer*, collected near Perth, on extraction with light petroleum, also yields methylheptenone and iridodial. Methylheptenone was again confirmed by paper chromatography of the crude 2,4-dinitrophenylhydrazone. Methylheptanolone was not detected.

The Argentine ant, *I. humilis*, collected near Perth, on extraction with light petroleum, has yielded iridomyrmecin, the crystalline, optically active lactone, $C_{10}H_{16}O_2$, previously reported by Pavan (1949).

I. nitidus, collected near Sydney, has a characteristic "cocoanut" odour and, on extraction with light petroleum, has yielded a crystalline, optically active lactone, $C_{10}H_{16}O_2$, which is not identical with iridomyrmecin. We have named this compound iridolactone. It is soluble in cold sodium hydroxide solution, being reformed on the addition of mineral acid. Reaction with hydrazine

hydrate gives the hydrazide of the corresponding hydroxy acid, $C_{10}H_{18}O_3$. No carbonyl compounds were detected from *I. humilis* or *I. nitidus*.

Hot aqueous sodium hydroxide solution readily effects the conversion of iridodial into iridolactone. Such rearrangements are typical of 1,5-dialdehydes (cf. Hall 1954).

The insecticidal activities of the above extractives are being evaluated by Mr. R. W. Kerr (Division of Entomology, C.S.I.R.O., Canberra). A preliminary examination of *I. rufoniger* (Lowne), *I. gracilis* (Lowne), and *I. gracilis* var. *rubriceps* (Forel) indicates the presence of terpenoid constituents. It is intended to characterize these compounds when further supplies of ants are available. Degradative studies on iridodial and the related iridolactone are in progress.

III. EXPERIMENTAL

Melting points are uncorrected. Light petroleum has b.p. 40–60 °C. Carbon, hydrogen, and nitrogen microanalyses are by Dr. E. Challen and Mr. D. Weedon of this University. Additional analyses were carried out by C.S.I.R.O. Microanalytical Laboratory.

(a) *Steam Distillation of I. detectus*.—The meat ants, stored in absolute ethanol, were air dried (450 g), then added to water (2 l.), and pulped. A pleasant "ester" odour was immediately noticeable on maceration. Steam distillation of the pulp gave a colourless homogeneous liquid (neutral to litmus) containing some ethanol. The distillate, after saturation with common salt, was extracted with light petroleum and the non-aqueous layer separated, washed (water), and dried (anhyd. $MgSO_4$). Removal of the solvent yielded a colourless oil which, on distillation, gave 2-methylhept-2-en-6-one (II) (3.5 g), b.p. 170–172 °C/755 mm, n_D^{20} 1.4420 (Found: C, 76.6; H, 10.9%. Calc. for $C_8H_{14}O$: C, 76.1; H, 11.2%). The ketone gave a positive iodoform reaction and decolorized bromine in carbon tetrachloride. The semicarbazone, prepared in the usual manner, was obtained as colourless plates, m.p. 136–137 °C, from aqueous ethanol (Found: C, 59.1; H, 8.8; N, 22.6%. Calc. for $C_8H_{17}ON_3$: C, 59.0; H, 9.4; N, 22.9%). A mixed m.p. with an authentic specimen showed no depression. The 2,4-dinitrophenylhydrazone was isolated as yellow needles, m.p. 86 °C, from light petroleum (Found: C, 54.8; H, 5.9; N, 18.5%. Calc. for $C_{14}H_{18}O_4N_4$: C, 54.9; H, 5.9; N, 18.3%). Mixed m.p. with an authentic specimen was not depressed.

On several occasions, the methylheptenone fraction yielded a mixture of 2,4-dinitrophenylhydrazones which were resolved by chromatography on alumina. Elution with benzene gave the methylheptenone 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 86 °C, then benzene-chloroform (4:1) yielded 2-methylheptan-2-ol-6-one 2,4-dinitrophenylhydrazone, recrystallized from chloroform-light petroleum as orange needles, m.p. 113 °C (Found: C, 51.9; H, 6.4%. Calc. for $C_{14}H_{20}O_4N_4$: C, 51.8; H, 6.2%). A mixed m.p. with an authentic specimen (see Section III (b)) showed no depression.

(b) *Methylheptanolone and Related Compounds*.—Methylheptenone (50 g), obtained from citral by the method of Verley (1897), was added to dilute sulphuric acid (500 g; 50% w/v) at 25–35 °C. The resultant pale yellow solution was neutralized with 10N sodium hydroxide solution, when a viscous oil (56 g) separated. After drying (anhyd. K_2CO_3), distillation gave the methylheptanolone as a colourless oil (50 g), b.p. 87–90 °C/10 mm, n_D^{20} 1.4445. The hydration process is a modification of that originally described by Verley (loc. cit.), who reported considerable decomposition during distillation.

2-Methylheptan-2-ol-6-one 2,4-dinitrophenylhydrazone was prepared from the above keto alcohol, being obtained from benzene-light petroleum as orange needles, m.p. 115 °C (Found: C, 51.6; H, 5.7; N, 17.4%. Calc. for $C_{14}H_{20}O_4N_4$: C, 51.8; H, 6.2; N, 17.3%).

Dehydration of methylheptanolone (1.9 g) by the method of Verley (loc. cit.) gave 2,6,6-trimethyl-5,6-dihydropyran (1.3 g) isolated as a colourless oil, b.p. 130 °C, n_D^{22} 1.4424. The dihydropyran, on treatment with aqueous 2,4-dinitrophenylhydrazine sulphate solution, readily

precipitated the identical 2-methylheptan-2-ol-6-one 2,4-dinitrophenylhydrazone, recrystallized from benzene-light petroleum as orange needles, m.p. and mixed m.p. 114–115 °C.

(c) *Solvent Extraction of I. detectus*.—The whole ants (1270 g, air dried after removal of storage ethanol) were Soxhlet extracted with light petroleum (56 hr). Removal of the solvent gave an amber oil (150 g) which, on fractional distillation under reduced pressure, has yielded: (i) methylheptenone (50 g), b.p. 60 °C/3 mm, (ii) a pale yellow oil (19.8 g), b.p. 104–108 °C/4 mm, and (iii) a residual fat fraction (50 g).

(i) 2-Methylhept-2-en-6-one, after standing over anhydrous calcium chloride, was redistilled as a colourless liquid, b.p. 168–170 °C (Found: C, 76.0; H, 11.2%. Calc. for $C_9H_{14}O$: C, 76.1; H, 11.2%). The infra-red spectrum of this compound was identical with that of methylheptenone prepared from citral (see Section III (b)). The semicarbazone, prepared as in Section III (a), had m.p. and mixed m.p. 136–137 °C.

(ii) Refractionation of the oil (19.8 g) has yielded *iridodial* (16.1 g), as a colourless liquid, b.p. 90–92 °C/1.0 mm (Found: C, 71.2; H, 9.4%. Calc. for $C_{10}H_{14}O_2$: C, 71.4; H, 9.6%). A fresh sample (0.5 hr) had n_D^{19} 1.4782; sp. gr. $^{19}_4$ 1.001; M.R. (Lorentz-Lorenz) 47.5. Iridodial readily polymerized to a glassy mass but was depolymerized on heating (oil-bath at 120 °C) and redistilled as a colourless oil, b.p. 56–57 °C/0.08 mm (Found: C, 71.0; H, 9.4%. Calc. for $C_{10}H_{14}O_2$: C, 71.4; H, 9.6%).

Reaction, in 50% ethanol, with aqueous 2,4-dinitrophenylhydrazine sulphate solution, gives an instantaneous precipitate of the *bis*-2,4-dinitrophenylhydrazone, finally isolated as pale orange needles, m.p. 224–225 °C (decomp.) from ethyl acetate (Found: C, 49.8, 50.1; H, 4.6, 4.6; N, 21.5, 21.2%; mol. wt. (Rast), 556. Calc. for $C_{22}H_{24}O_8N_8$: C, 50.0; H, 4.6; N, 21.2%; mol. wt., 528).

Iridodial di-semicarbazone, prepared in the usual manner, was finally obtained from ethanol as colourless needles, m.p. 192 °C (decomp.) (Found: C, 51.3; H, 7.9; N, 29.9%. Calc. for $C_{12}H_{22}O_2N_6$: C, 51.0; H, 7.9; N, 29.8%). The ultraviolet absorption spectrum of this derivative, measured in 95% ethanol, shows the characteristic peak of a simple semicarbazone, λ_{max} 230 m μ , ϵ 24,600.

(d) *Potassium Permanganate Oxidation of Iridodial*.—Iridodial (2.34 g, freshly distilled) in 5% sodium hydroxide solution (30 ml) was oxidized with potassium permanganate (3.73 g) slowly added at 10 °C, over a period of 2 hr. The green reaction mixture which became colourless after standing overnight, was filtered to remove manganese dioxide. Extraction of the alkaline filtrate with ether (25 ml) gave a neutral oil (0.3 g). Acidification of the remaining pale yellow solution (dil. HCl) gave a lactic fraction (0.35 g), readily separated from a viscous yellow acid fraction (1.25 g). The mixture of acids gives no precipitate with 2,4-dinitrophenylhydrazine sulphate solution and no iodoform reaction. Attempts at recrystallization have not proved successful. A benzene-soluble fraction of these acids (0.45 g, equiv. wt. 103), as the neutral sodium salt, was heated under reflux (3 hr) with *p*-bromophenacylbromide (1.3 g) in the usual manner. The *bis*-*p*-bromophenacyl ester (0.62 g), thus obtained, was crystallized as colourless needles, m.p. 125–125.5 °C, $[\alpha]_D^{18}$ –15° (c, 1.12 in chloroform), from aqueous ethanol (Found: C, 52.3; H, 4.2%. Calc. for $C_{28}H_{26}O_6Br_2$: C, 52.5; H, 4.4%).

(e) *Extraction of I. conifer*.—The stick ants (450 g, air dried) were Soxhlet extracted with light petroleum as in Section III (c). The petroleum extract, after washing (water) and drying (anhyd. $MgSO_4$), was evaporated to yield a brown oil (24 g). Distillation of this oil gave: (i) Methylheptenone (0.7 g, crude), redistilled as a colourless oil, b.p. 171–172 °C, n_D^{20} 1.4419; readily forming the semicarbazone, m.p. and mixed m.p. 137–138 °C (Found: C, 58.8; H, 9.3; N, 22.8%. Calc. for $C_9H_{11}ON_3$: C, 59.0; H, 9.4; N, 22.9%).

(ii) Iridodial (0.85 g, crude), was identified by conversion into the *bis*-2,4-dinitrophenylhydrazone, finally obtained from benzene-light petroleum as yellow needles, m.p. and mixed m.p. 225–227 °C (decomp.) (Found: C, 50.3; H, 4.9; N, 21.2%. Calc. for $C_{22}H_{24}O_8N_8$: C, 50.0; H, 4.6; N, 21.2%).

No other volatile products were detected but a considerable fat fraction remained. A further quantity of oil (2.1 g) was isolated on evaporation of the storage ethanol; this oil yielded methylheptenone (0.4 g), identified as the 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 85–86 °C.

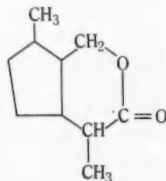
(f) *Extraction of I. nitidus*.—The whole ants (40 g) were Soxhlet extracted in the usual manner; the light petroleum in which the ants were collected was used as solvent. The extraction, worked up as in Section III (e), yielded an amber oil (3.5 g), which on distillation gave *iridolactone* (2.5 g), b.p. 97 °C/0.6 mm, which rapidly solidified on cooling. Iridolactone was finally isolated as colourless needles, m.p. 58–59 °C, $[\alpha]_D^{17} -62^\circ$ (c, 1.01 in carbon tetrachloride) (Found: C, 71.6; H, 9.7; O, 19.4%; mol. wt. (Rast), 184. Calc. for $C_{10}H_{16}O_2$: C, 71.4; H, 9.6; O, 19.0%; mol. wt., 168). Iridolactone is soluble in dilute sodium hydroxide solution, being recovered, by extraction with light petroleum, after acidification with dilute hydrochloric acid, m.p. and mixed m.p. 58–59 °C.

Iridolactone (150 mg) in absolute ethanol (3-ml) was refluxed with hydrazine hydrate (1 ml; 100%) for 2 hr. The solution was evaporated to smaller bulk and, on cooling, a crystalline solid was precipitated. The *hydrazide* of the hydroxy acid crystallized from benzene as colourless needles (50 mg), m.p. 118–119 °C (Found: C, 60.1; H, 10.3; N, 14.0%. Calc. for $C_{10}H_{20}O_2N_2$: C, 60.0; H, 10.1; N, 14.0%).

(g) *Action of Alkali on Iridodial*.—Iridodial (1.78 g) in sodium hydroxide solution (25 ml; N) was heated on the water-bath, when only a trace of material remained undissolved after 1 hr. Back-titration with N hydrochloric acid solution (phenolphthalein) indicated 95% conversion to the hydroxy acid. The remaining neutrals (0.13 g) were extracted with ether. The aqueous solution, on acidification with excess hydrochloric acid, precipitated fine colourless needles (presumably the hydroxy acid), m.p. 106–107 °C. Extraction of this product with light petroleum effected lactonization of the hydroxy acid. The lactone fraction (1.2 g), obtained as an almost colourless oil, gave iridolactone (0.36 g), m.p. and mixed m.p. 57.5–58 °C, $[\alpha]_D^{19} -64^\circ$ (c, 1.0 in carbon tetrachloride) on repeated recrystallization from light petroleum (cf. Section III (f)).

(h) *Extraction of I. humilis*.—The Argentine ants (65 g, air dried after removal of ethanol in which they were collected) were Soxhlet-extracted with light petroleum, as in Section III (e). The extract, worked up as in (e), yielded an amber oil (8.0 g), which on distillation gave iridomyrmecin (0.2 g), b.p. 104–108 °C/1.5 mm, rapidly solidifying. Iridomyrmecin was recrystallized from light petroleum as colourless prisms, m.p. 59–60 °C, $[\alpha]_D^{17} +205^\circ$ (c, 0.223 in carbon tetrachloride) (Found: C, 71.4; H, 9.6%. Calc. for $C_{10}H_{16}O_2$: C, 71.4; H, 9.6%). A fatty residue was not distilled. Fusco, Trave, and Vercellone (1955) record m.p. 60–61 °C, $[\alpha]_D +210^\circ$ (c, 4.0 in ethanol).

An examination of the storage ethanol shows the presence of additional, light petroleum soluble, extractives (4.2 g), from which iridomyrmecin (0.2 g), m.p. and mixed m.p. 59 °C, has been isolated.



(i) *Paper Chromatography*.—The separation of the crude 2,4-dinitrophenylhydrazones was achieved on Whatman No. 1 paper, employing as solvent a hydrocarbon-rich phase, obtained by shaking a light petroleum fraction (b.p. 80–100 °C) with methanol in the ratio 2:1 (v/v). The solvent system is essentially that described by Huelin (1952). The chromatogram was run using the horizontal technique (4–6 hr). R_F values of the same derivative (i.e. methylheptenone 2,4-dinitrophenylhydrazone) varied slightly in different runs and thus the derivatives were always identified by running them alongside synthetic specimens in the same chromatogram. The

2,4-dinitrophenylhydrazones of natural methylheptenone (from solvent extraction of the whole ants, *I. detectus* and *I. conifer*) and the synthetic compound gave identical R_F values (c. 0.9). Methylheptanolone 2,4-dinitrophenylhydrazone (R_F c. 0.3), present in the methylheptenone fraction (from steam distillation of *I. detectus*) was not found in specimens isolated by solvent extraction.

Note Added in Proof.—Professor R. Fusco of the University of Milan, has recently advised us that iridomyrmecin (cf. I) has structure III. Stereochemically, it is related to nepetalactone (McElvain and Eisenbraun 1955).

IV. ACKNOWLEDGMENTS

The authors thank Dr. D. F. Waterhouse and Mr. T. Greaves (Division of Entomology, C.S.I.R.O., Canberra) for their interest and helpful discussion. We are also indebted to Mr. T. Greaves and other officers of the Division of Entomology, to Mr. A. Douglas (Perth Museum), and to Mr. J. Freeland (Como, N.S.W.) for supplies of ants. The Rev. Father J. J. McAreavey (Xavier College, Kew, Vict.) is thanked for his kind assistance in the classification of *Iridomyrmex* spp.

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SHORT COMMUNICATIONS

LIPID-WATER PARTITION COEFFICIENTS OF SOME PHENOTHIAZINES*

By J. CYMERMAN-CRAIG† and W. K. WARBURTON‡

The well-known anthelmintic phenothiazine possesses extremely low water-solubility, stated as 1 part in 800,000 by Davey and Innes (1942). It has been shown that phenothiazine enters nematode parasites largely through the cuticle (Lazarus and Rogers 1951). Since one of the factors influencing the permeability of a cell membrane to a drug molecule must be the lipid-water partition coefficient of the drug, it was of interest to determine this constant for a number of substituted phenothiazines.

Method

Solubilities in water were too low to allow the method of Cymerman-Craig and Diamantis (1953) to be used. Accordingly, absolute solubilities were determined in water (S_w) and in *n*-heptane (S_L). Water was buffered to pH 6.5 with phosphate buffer (Clark 1928). *n*-Heptane (b.p. 98–99 °C) was obtained spectroscopically transparent by repeated treatment with chlorosulphonic acid.

S_L was determined by shaking an excess of the finely ground compounds with heptane at 20 ± 2 °C for 48 hr, filtering rapidly without suction, and diluting the filtrate to a concentration (usually 1 in 250) which gave a convenient value of the optical density d at the wavelength of maximum absorption. Comparison with the values of d in heptane for known concentrations gave the absolute solubility. The agreement with Beer's law was very close in all cases. S_w was determined by shaking the finely ground compound with M/120 phosphate buffer solution at 20 ± 2 °C for 48 hr, filtering without suction and extracting a known volume of the filtrate (usually 200 ml) with three portions of heptane, and making the heptane up to a known volume, usually 25 ml. Further extraction did not increase the optical density. Measurement of d and comparison with the standards enabled the concentration in water to be calculated. Duplicates for both S_L and S_w were within 10 per cent. Spectroscopic measurements were made with a Beckman model DU spectrophotometer in 1 cm quartz cells.

All samples were of analytical purity and had the highest m.p.'s recorded in the literature. The oxygen-sensitive 3-hydroxyphenothiazine was handled in an inert atmosphere.

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Results

Table 1 shows the partition coefficients obtained, together with the values of S_L and S_H , and the ultraviolet absorption maxima and intensities, for 18 phenothiazines.

Water-solubility is seen to decrease with increasing molecular complexity of the 3-substituent as expected, and the partition coefficients themselves show a 2 million-fold range, varying from 0.081 to 180,000. These results serve

TABLE 1
PARTITION COEFFICIENTS OF PHENOTHIAZINES

Phenothiazine	S_L (mg/100 ml)	S_H (mg/100 ml)	S_L/S_H	$\text{Log}_{10} \epsilon$	$\lambda_{\text{max.}}$ (m μ)
3-Hydroxy-	4.62	57.3	0.081	4.61	253
2,7-Dichloro-	0.675	0.0106	6.4	4.67	261
3,7-Dichloro-	0.292	0.0043	6.8	4.90	260
2-Chloro-7-methoxy-	7.70	0.277	26.2	4.87	253
3-Methoxy-	43.7	0.161	270	4.42	253
3,7-Dimethoxy-	7.45	0.011	680	4.45	254
3-Methyl-	76.5	0.0445	1700	4.62	255
3,4-Benzo-	11.5	0.00667	1700	4.36	241
3,4-6,7-Dibenzo-	7.90	0.00396	2000	4.67	268
3-Chloro-	31.4	0.0153	2100	4.62	258.5
3-Bromo-	86.5	0.0215	4000	4.67	258
3-Fluoro-	116	0.0280	4100	4.37	259
1,2-Benzo-	220	0.0317	6900	4.44	254
Unsubstituted	387	0.0510	7600	4.52	253
3-Iodo-	33.8	0.00384	8800	4.46	255
3,7-Dimethyl-	112	0.0094	12000	4.55	255
10-Methyl-	2083	0.0544	38000	4.60	255
1,2-8,9-Dibenzo-	68.0	0.00037	180000	4.51	252

to indicate the tremendous influence of substitution on partition coefficients in this series, but do not in themselves suggest any direct correlation between this property and anthelmintic activity.

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SOME OBSERVATIONS ON THE OXIDATION OF *iso*BUTANE AND PROPYLENE*

By M. J. RIDGE†

It has been observed that the addition of inert gas to *isobutane* undergoing low-temperature oxidation reduces the induction period, but has little effect upon the subsequent maximum rate of pressure change (Ridge 1956). The diminution of the induction period by inert gas suggests that its length is controlled by the rate of destruction of an active intermediate at the walls of the reaction vessel (Mulcahy and Ridge 1953*b*; Ridge 1956). From the change in the effect of inert gas after the induction period it is clear that in the oxidation of *isobutane* the reaction producing the main increase in pressure depends on the nature of the surface in a different way from the reaction which takes place during the induction period. A study of the progressive accumulation of products during the reaction supports this view, and the total evidence at hand strongly suggests that effects of the condition of the surface are of secondary importance after the induction period (Batten, Gardner, and Ridge 1955). However, it is general experience that a reduction in the induction period due to a change in the condition of the surface is accompanied by an increase in the maximum rate.

This note records some observations regarding the effect of changes in the condition of the surface of the reaction vessel on the maximum rate of the oxidation of *isobutane* and of propylene, and also the effect of inert gas in the oxidation of propylene. It is found that inert gas has little effect upon the maximum rate in the oxidation of propylene. This is in accord with the results for *isobutane*. It is also found that in the oxidations of both propylene and *isobutane* changes in the condition of the surface influence the maximum rate and induction period to nearly the same extent. It is suggested that the effect of surface on the maximum rate is a secondary effect arising from differences in the amounts of reagents consumed and products formed during induction periods of different lengths.

The apparatus and the preparation of the materials have already been described (Mulcahy and Ridge 1953*a*, 1953*b*; Batten, Gardner and Ridge 1955).

Results

Figure 1 shows the influence of the concentration of nitrogen P_{N_2} on the maximum rate ρ_{\max} of the mixture 50 mm propylene+350 mm oxygen at 291 °C for two conditions of surface activity.

(i) *The Effect of Inert Gas on the Maximum Rate in the Oxidation of Propylene.*—The lines of Figure 1 show that ρ_{\max} is very nearly independent of

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the pressure of nitrogen. Ten per cent. would be a generous estimate of the increase in the maximum rate for the addition of 300 mm of nitrogen. The corresponding effect on the reciprocal induction period is, for example, an increase from 0.0187 to 0.0305 min⁻¹, that is, an increase of 63 per cent. of its initial value. Hence it is clear that the maximum rate of the oxidation of propylene is much less sensitive than the induction period to the concentration of inert gas. All observations so far made lead to the conclusion that the maximum rate is probably unaffected by the addition of inert gas.* This is in accord with previous observations for the oxidation of *isobutane* (Ridge 1956).

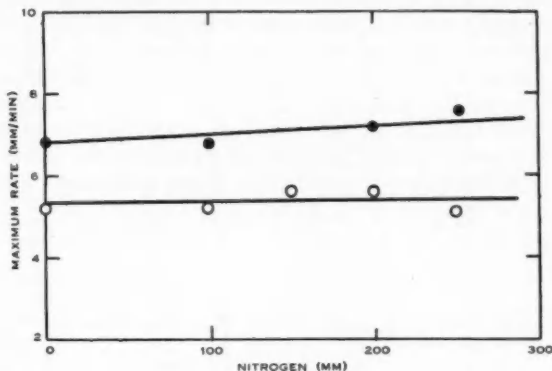


Fig. 1.—The influence of the concentration of nitrogen on the maximum rate of pressure change, p_{\max} , for the reaction mixture 50 mm propylene + 350 mm oxygen at 291 °C at two different conditions of the surface of the reaction vessel.

○ Induction period at zero concentration of nitrogen, 70.5 min.

● Induction period at zero concentration of nitrogen 53.5 min.

(ii) *The Effect of Surface† on the Maximum Rate.*—The results of Figure 1 show an increase of c. 30 per cent. in the maximum rate of the oxidation accompanied by a decrease of c. 24 per cent. in the induction period for zero concentration of nitrogen, due to a change in the condition of the surface. This indicates that the maximum rate is about as sensitive as the induction period to changes in the condition of the surface. Similar effects were found in the oxidation of *isobutane* as is seen from Table 1.

* Owing to a more abrupt change in pressure at the end of the induction period the results for propylene are not quite as clear as those for *isobutane* (Ridge 1956).

† Variations in the activity of the surface were not brought about by any special treatment. The activity of the surface may be kept constant during a set of experiments if a strict procedure in pumping and admitting the reagent is observed. During a period of rest the activity of the surface drifts. After a few runs the surface again settles down to a constant condition which is usually different from the previous one. The changes in the surface discussed in the present communication are of this type.

TABLE I
EFFECT OF SURFACE ON THE MAXIMUM RATE OF PRESSURE INCREASE OF 80 MM ISOBUTANE AND
350 MM OXYGEN AT 291 °C

Induction period (min)	62	30	27
Maximum rate (mm/min)	9	15	16, 18

Discussion

It has been shown that during the induction period appreciable quantities of reactants are converted into products (Batten, Gardner, and Ridge 1955 ;

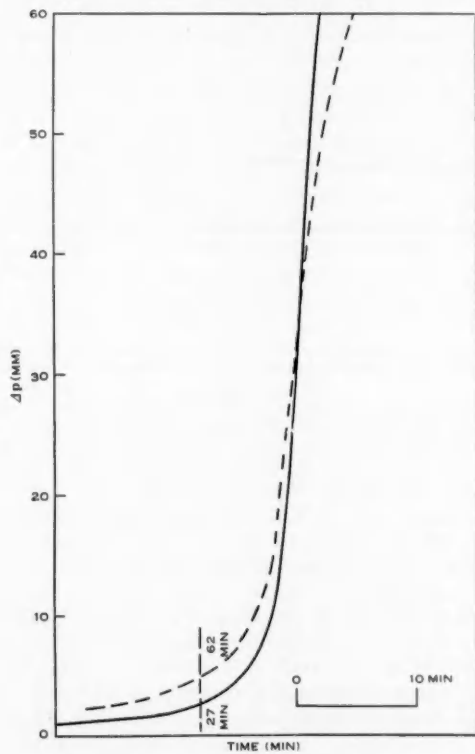


Fig. 2.—Increase in pressure Δp v. time for 80 mm iso-butane + 350 mm oxygen at 291 °C.

Curve — induction period 27 min.

Curve - - induction period 62 min.

The two curves have been shifted relatively to one another along the time axis, so that the ends of the induction period are coincident.

Mulcahy and Ridge 1953a). Some of these products have a catalytic effect (either positive or negative), for example, formaldehyde, which acts as an

inhibitor after the induction period for the oxidation of both *isobutane* and propylene (Batten and Ridge 1955).

It has been suggested that the reaction during the induction period is a straight chain process which is eventually overshadowed by an autocatalytic reaction initiated by a product which accumulates during the induction period (Batten and Ridge 1955). If the induction period is lengthened owing to a more reactive surface reducing the rate of accumulation of the agent of degenerate branching, more of the reagents will be consumed and more products formed during the induction period. This will result in a reduction of the maximum rate and this change in the maximum rate would be a secondary effect of the change in the surface activity. The effect is illustrated in Figure 2, which shows the pressure-rise *versus* time curves for 80 mm *isobutane*+350 mm oxygen for two separate reactions in which different activities of the surface resulted in the induction periods being 62 min in one case and 27 min in the other. It is seen that the increase in pressure at the end of the 62 min induction period is twice that at the end of the 27 min induction period, indicating a considerable difference in the amount of reactants converted to products during the induction period.

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BENZENE-METHANOL AS A SOLVENT IN AROMATIC NUCLEOPHILIC SUBSTITUTION*

By R. L. HEPPLETTE,† I. R. LANTZKE,† and J. MILLER†

Most of the previous papers of Miller and co-workers considering aromatic S_N reactions have recorded measurements of rates of (the S_N2) reactions of aromatic compounds with OMe^- in absolute methanol. A few compounds were found which were insufficiently soluble in methanol alone, and benzene-methanol (50-50; v/v%) has been used as an alternative solvent.

To enable comparisons to be made it was then necessary to investigate the methanolysis of at least one standard substance in MeOH and in the mixed solvent. A substance much investigated in aromatic S_N reactions is 1-chloro-2,4-dinitrobenzene, and the methanolysis of this in a whole range of C_6H_6 -MeOH mixtures was investigated, so that some explanation of the effect of added C_6H_6

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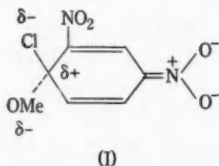
might also be attempted. In addition, two other compounds were investigated in MeOH and C_6H_6 -MeOH (50-50; v/v%). These were 4-chloro-3-nitrophenyl-methylsulphone and 4-chloro-3-nitrobenzophenone. The three compounds are all of the type 4-Cl-3- NO_2 - C_6H_3X , where X is a $-I-T$ group, and the experimental results are given as Table 1.

Discussion

It was found difficult to obtain the same accuracy and reproducibility with reactions in C_6H_6 -MeOH as in MeOH alone, however, the following conclusions may be drawn: (i) the effect of added C_6H_6 on rates is small; (ii) the simple Hughes-Ingold theory of solvent action (Hughes and Ingold 1935) is not obeyed—it predicts a small increase in rates (cf. Briner and Miller 1954); (iii) in the range of solvents tested with 1-chloro-2,4-dinitrobenzene, there is a minimum in rates in the region of 20 per cent. C_6H_6 (mole fraction 0.10).

The Arrhenius parameters indicate a greater effect of added C_6H_6 than is suggested by rate changes. The rate minimum at 20 per cent. C_6H_6 is consequent on a drop in the frequency factor (entropy term) overcompensating a drop in activation energy. The reduction in both the terms suggests that the transition state, thought to be most nearly represented by structure I (Bunnett and Zahler 1951; Miller 1951; Bolto and Miller 1956), is more strongly solvated in 20-80 (v/v%) C_6H_6 -MeOH than in pure MeOH or other C_6H_6 -MeOH mixtures. This may be compared with the results of Tommila and Merikallio (1953), Tommila and Hella (1954), Tommila and Kauranen (1954), and Tommila, Tiilikainen, and Voipio (1955), who in their investigations of ester hydrolysis in mixed solvents also found similar minima.

More specifically, with OMe^- more strongly solvated by MeOH and the aromatic compound by C_6H_6 , the transition state I, containing centres preferentially solvated by both components of the mixed solvent, could be solvated



more than either reactant, and thus lead to the observed result. However, the explanation is only qualitative and the most effective relative concentrations are not predictable.

In the solvent containing most C_6H_6 the dielectric constant (D) may be estimated as about 17 (assuming a linear relationship between mole fractions and D) so that the solvents cover a range in D of about 17-33. In such solvents the formation of ion pairs or ion clusters must be considered possible, and minima in electrical conductivities of salts in solvents of low dielectric constant may be ascribed to such ion association. However, for solutions of salts in mixed solvents with MeOH as one component in particular, it is known that the addition to MeOH of, for example, C_6H_6 causes an increase in dissociation,

TABLE 1
METHANOLYSIS OF 4-SUBSTITUTED 1-CHLORO-2-NITROBENZENES

4-Sub- stituent	Solvent		Mole Fraction C_6H_5	Rate Constants 10^4k_2 (l mole ⁻¹ sec ⁻¹)				Rate Ratio $MeOH/C_6H_5 \cdot MeOH$ at:		Activation Energy, E (k cal)	Frequency Factor, $\text{Log}_{10} B$	
	MeOH	C_6H_5		(a) At Temperatures Shown in Parentheses	(b) Calc. at:		0 °C	50 °C	0 °C			50 °C
					0 °C	50 °C						
NO_2 ..	100	0	0	Beckwith, Miller, and Leahy (1952)	200	2.88×10^4	1	1	17.4 _s	11.2 _s		
	80	20	0.10	190 394 478 2390 2370 (0) (6.6) (8.2) (24.8) (25.15)	192	1.95×10^4	0.96	0.68	16.2 _s	10.3		
	50	50	0.31	208 427 750 1710 3010 (0.2) (6.2) (11.0) (19.1) (25.2)	200	3.0×10^4	1.00	1.04	17.5	11.3		
	30	70	0.51	178 435 579 563 2490 (0) (7.8) (10.25) (10.4) (24.8)	180	2.4×10^4	0.90	0.83	17.1 _s	11.0		
SO_2Me ..	100	0	0	61.2 97.8 288 830 1990 (11.4) (15.5) (25.0) (35.6) (45.0)	15.7	3.22×10^3	1	1	18.6 _s	11.1		
	50	50	0.31	195 314 529 912 2200 (20.05) (24.9) (29.9) (35.4) (44.9)	19.3	3.45×10^3	1.23	1.07	18.2	10.8 _s		
OPh ..	100	0	0	Miller (1954)	3.79	668	1	1	18.1 _s	10.1		
	50	50	0.31	169 252 384 428 1220 (35.4) (40.1) (44.9) (46.2) (59.6)	4.74	581	1.25	0.87	16.8 _s	9.1 _s		

regarded as consequent on depolymerization of the (hydrogen bonded) MeOH (Mecke 1950; Sacks and Fuoss 1953), so that the solutes become ideal strong electrolytes. It is felt in any case that an explanation of rate minima, as found here, involving such ion association would not be applicable in these reactions, where one species is attacked by an anionic species in solvents which contain a large excess of the conjugate acid of the anionic reagent. Further, the mixed solvents may be inhomogeneous in the sense that the solvent in the vicinity of solute species may be somewhat different from the composition of the bulk solvent.

In the solvents investigated, the data for the SO_2Me compound are very similar to those of the NO_2 as expected for a dipolar $-I-T$ group.

While the rates are again little affected the reduced values of the Arrhenius parameters for the COPh compound in 50-50 (v/v%) C_6H_6 -MeOH probably reflect the effect of the extra Ph group, but unfortunately the results for this compound are not very reliable (see *Experimental* Section). Nevertheless it is relevant to note that Bolto and Miller (unpublished data) recorded an even larger drop in both activation energy and frequency factor for a Ph group attached direct to a similar system, and that there also results in the mixed solvent could not be relied on. The effect of an additional Ph group is not therefore being pursued further at present.

Experimental

Kinetic runs were followed by "quenching" aliquots in a standard acid (HCl or chloride-free HNO_3), and either back-titrating excess acid using brom-cresol green/methyl red as indicator, or estimating chloride potentiometrically. The values of k_2 were obtained graphically.

Acid-base titration end-points were difficult to observe precisely in C_6H_6 containing solvents without the utmost care, while for runs followed by estimation of chloride it was necessary either to add sufficient MeOH to obtain a homogeneous titration mixture or to evaporate the C_6H_6 off in a fume-hood.

The k_2 plots for the COPh compound in C_6H_6 -MeOH were not linear but curved in the direction corresponding to k_2 increasing during the runs. Also, whereas in MeOH alone the product was the pure methoxy compound, a mixture of products was obtained from C_6H_6 -MeOH runs; but neither benzophenone nor *m*-nitrobenzophenone appear to react with OMe^- in C_6H_6 -MeOH (50-50; v/v%) in the conditions in which some side reaction appears to occur with 4-chloro-3-nitrobenzophenone. The k_2 values quoted for this compound are those obtained from the initial slopes of the k_2 curves, and while reliable enough to show that added C_6H_6 has little effect on rates are not considered good enough to estimate with any certainty the effect of the additional Ph group.

For each compound, rate constants were measured at five temperatures, some in duplicate, and the Arrhenius parameters obtained by a least squares analysis of corresponding values of $\log_{10} k_2$ and reciprocal temperature. Estimated probable errors are ± 400 -500 in E and ± 0.3 -0.4 in $\log B$ for the NO_2 and SO_2Me compounds. The error for the COPh compound in C_6H_6 -MeOH is difficult to estimate, but would be at least double this.

Preparation of Materials

1-Chloro-2,4-dinitrobenzene.—As prepared by Beckwith, Miller, and Leahy (1952).

Sodium-p-Chlorobenzene Sulphinate.—The acid was formed (Todd and Shriner 1934) by the Cu bronze catalysed action of SO_2 on the diazonium salt formed from *p*-chloroaniline. It was purified as the sodium salt, and obtained in 38 per cent. overall yield.

p-Chlorophenylmethyl Sulphone.—Methyl iodide (3.5 ml) was reacted with sodium *p*-chlorobenzene sulphinate (13 g) in ethanol (300 ml). By concentration of the mixture the product was obtained in 81 per cent. yield, and after recrystallization from water had m.p. 96°C (lit. 96°C).

4-Chloro-3-nitrophenylmethyl Sulphone.—By nitration of *p*-chlorophenylmethyl sulphone analogously to the nitration of *p*-chlorobenzaldehyde by Hodgson and Beard (1927). Potassium nitrate (6 g) was added to the sulphone (8 g), dissolved in conc. H_2SO_4 (20 ml), and the temperature kept at 70°C for 2 hr. After cooling and pouring on to crushed ice the product was obtained in 59 per cent. yield. After recrystallization from MeOH it melted at 123.5°C (lit. 119 – 120°C). At the time of preparation this compound had not been reported in the literature, but a slightly different preparation and rate constants for reaction with OMe^- in MeOH have been reported by Bunnett *et al.* (1953).

4-Chloro-3-nitrobenzophenone.—As prepared by Miller (1954).

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CORRIGENDA

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Page 77, structural diagram: In transition state 1, a dotted line should be drawn from Y^- to the ring at the point of attachment of X . In transition state 2, a dotted line should be drawn from X^- to the ring at the point of attachment of Y . These are to indicate that the electrostatic type bonds also have some covalent character, the extent of which will vary with the system.

Page 78, for 3rd paragraph from bottom commencing "The above discussion . . ." substitute the following:

"The above discussion is tentative, but if valid would lead to the conclusion that the Arrhenius parameters for the compound $X=NO_2$ would have values between those for $X=F$ and SMe_2^+ , and not resemble those for $X=NMe_3^+$, while the main difference between $X=Cl$ and F would be in the activation energy (F lower). These conclusions are confirmed by experiment."

